DISSERTATION

on

PREVALENCE AND EVALUATION OF HYPONATREMIA IN ELDERLY PATIENTS

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CERTIFICATE

This is to certify that the dissertation titled **"PREVALENCE AND EVALUATION OF HYPONATREMIA IN ELDERLY PATIENTS"** is a bonafide work done by **Dr. A. KARTHIKEYAN**, Post Graduate Student, Department of Geriatric Medicine, Madras Medical College, Chennai – 600003, in partial fulfillment of the university rules and regulations for the award of MD DEGREE in GERIATRIC MEDICINE BRANCH-XVI, under our guidance and supervision, during the academic period from April 2010 to April 2013.

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DECLARATION

I solemnly declare that the dissertation titled **"PREVALENCE AND EVALUATION OF HYPONATREMIA IN ELDERLY PATIENTS"** was done by me at Madras Medical College, Chennai – 600003, during the period June 2012 to December 2012 under the guidance and supervision of **Prof. B. KRISHNASWAMY, MD**, to be submitted to The Tamil Nadu Dr. M.G.R. Medical University towards the partial fulfillment of requirements for the award of MD DEGREE in GERIATRIC MEDICINE BRANCH-XVI.

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ABBREVIATIONS

ACE Angiotensin Converting Enzyme

ADH Anti Diuretic Hormone

ADPKD Autosomal Dominant Polycystic Kidney Disease

ANH Atrial Natriuretic Hormone

AVP Arginine VasoPressin

BP Blood Pressure

BUN Blood Urea Nitrogen

CCF Congestive Cardiac Failure

CRF Chronic Renal Failure

ECF Extra Cellular Fluid

ESRD End Stage Renal Disease

GFR Glomerular Filtration Rate

ICF Intra Cellular Fluid

JVP Jugular Venous Pressure

MCD Minimal Change Disease

NSAIDS Non Steroidal Anti Inflammatory Drugs

NTS Nucleus Tractus Solitarius

OVLT Organum Vasculosum of Lamina Terminalis

RAAS Renin Angiotensin Aldosterone System

RPF Renal Plasma Flow

SAH Sub Arachnoid Hemorrhage

SIADH Syndrome of Inappropriate Anti Diuretic Hormone Secretion

TBW Total Body Water

ABBREVATIONS FOR MASTER CHART

HEV Hypervolemic

EV Euvolemic

HOV Hypervolemic

HYPOT Hypothyroism

NPHR Nephrotic syndrome

CCF Congestive cardiac failure

PCRT Pancreatitis

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INTRODUCTION

Elderly are vulnerable to electrolyte disturbances, hyponatremia being the commonest disorder in the aged population [1]. It is defined as plasma sodium level below 135 mEq/litre. Many studies show that hyponatremia is prevalent in the hospitalized patients in around 20 percent. Incidence of hyponatremia is higher among elderly, when compared to young adults. This is attributed to the fact that, when elderly persons are exposed to a change in environment and an altered dietary practice, there is impairment in their ability to maintain an optimal balance of water and electrolytes [2].

Factors contributing to the development of hyponatremia in the elderly patients include an age associated decrease in free water excretion and glomerular filtration rate (GFR). Aging is associated with increased loss of sodium in urine. This is contributed by decreased action of renin angiotensin aldosterone system (RAAS) and exaggerated action of natriuretic hormones.

Development of severe hyponatremia is associated with high morbidity and mortality. This is especially so in elderly patients. Hence identification and assessment of different types of hyponatremia in elderly patient is very important to improve the patient outcome. The etiology of hyponatremia among geriatric age group is complex and it is

further complicated by an unclear relationship between arginine vasopressin and advancing age

There are different types of hyponatremia based on the volume status of the individual. They are

1. Euvolemic hyponatremia
2. Hypervolemic hyponatremia
3. Hypovolemic hyponatremia

Particularly in hospital setting with acute medical problems, the recognition of different types of hyponatremia and appropriate clinical intervention is critical for improving patient outcomes. Data regarding the prevalence and different types of hyponatremia in elderly in our country is limited.

History and clinical examination including assessment of volume status, measuring serum osmolality, serum sodium and urinary sodium concentrations is essential to differentiate the types of hyponatremia and to detect the possible etiological factor responsible for hyponatremia and to determine the most appropriate treatment.

AIMS OF THE STUDY

1. To identify the prevalence of hyponatremia in hospitalized elderly patients above 65 years of age.
2. To study the clinical presentation of hyponatremia in elderly.
3. To identify the types and etiological factors of hyponatremia.

REVIEW OF LITERATURE

Hyponatremia is defined as plasma sodium below 135 mEq/litre. This results from an increase in circulating arginine vasopressin and increased renal sensitivity to arginine vasopressin, combined with free water intake. Homeostatic system regulating water and electrolyte balance undergoes various changes with age. The confluence of aging, associated medical conditions, multiple drug intake, varied oral intake, results in water and electrolyte abnormalities in the elderly.

PREVALENCE:

Hyponatremia is the most common electrolyte abnormality in geriatric age group [4]. Prevalence of hyponatremia in chronic care facilities is 15 to 18 percent [5]. Studies suggest a one percent prevalence of hyponatremia in nursing home residents.[6]. A study conducted by Gill's et al showed a mortality of 28 percent when plasma sodium falls below 125 mEq/litre [7]. It is said that the prevalence of hyponatremia is 18 percent in a study conducted among nursing home resident [8]. When these residents are observed over a period of one year ,53 percent of the observed experienced one or more episodes of hyponatremia [8]

BODY COMPOSITION OF FLUIDS:

About 55 to 65 percent of body weight is constituted by total body water [TBW]. Total body water is divided and distributed into intracellular [ICF] and extracellular [ECF] fluid compartment. 55 to 75 percent of total body water is in ICF and 25 to 45 percent is in ECF. ECF is subdivided into intravascular and interstitial fluid in the ratio of 1:3.That is 75 percent of ECF is in interstitial fluid and 25 percent is in intravascular compartment. Sodium is primarily an extracellular cation and potassium is primarily an intracellular cation.

EFFECTS OF AGING IN BODY COMPOSITION:

Normal aging is associated with a decrease in total body water, decrease in muscle mass and there is higher fat mass. Thus, TBW declines approximately from 60 percent of body weight to 53 percent in men older than age of 65 years when compared to young adults. TBW in women older than age of 65 years decreases from 52 percent of body weight to 45 percent when compared to young adults. This is mainly due to decline in ICF. This decrease in TBW may place the elderly patient at risk of hyponatremia.

WATER HOMEOSTASIS:

The maintenance of normal water balance is achieved through the combined action of three main factors: vasopressin, the kidney, and thirst mechanism. Equal amount of water intake and water loss is required for maintenance of water balance. Secretion of adequate quantities of osmotically stimulated vasopressin is needed, which must be able to bind to the renal tubule to modulate the flow of solute-free water and produce antidiuresis. Daily loss of water from an extra renal route is approximately 500ml. Daily loss of water from kidney depends on urinary solute excretion. Most healthy adults usually ingest 1.5 to 2.5 L of water per day and excrete 1 to 2 litres of urine per 24 h, but the normal kidney is capable of wide variation in urine output. Osmotically stimulated thirst must be able to promote drinking and is particularly important when the kidney is concentrating urine maximally.

Persistent water loss can occur from excessive sweating due to fever, exercise, hot climate or copious watery diarrhoea. Under these circumstances water homeostasis cannot be maintained without adequate fluid intake. The increase in serum osmolality due to this extrarenal water loss activates thirst centers and favours arginine vasopressin secretion. This promotes water intake and conserves water loss through kidney leading to restoration of water balance and maintaining a normal serum

osmolality. Fine control of water balance ensures that the concentration of solutes, particularly extracellular sodium, remains stable. These factors allows plasma osmolality to be maintained within the narrow range 285 to 295 mosm/kg of water in healthy adults.

ROLE OF THIRST IN WATER BALANCE:

Thirst is the defence mechanism to promote water intake in response to loss of body water. It is defined as consciously perceived desire for water. True thirst must be distinguished from other determinants of fluid intake such as taste, dietary preferences, and social customs. Hyperosmolality is the potent stimulus for thirst. Stimulus for thirst arises when serum osmolality is raised above 290 mosm/kg of water. Thirst centres are located in anterior hypothalamus. Hypovolemia stimulates renin angiotensin aldosterone system [RAAS], angiotensin II reaching the hypothalamus stimulates the thirst by potent dipsogenic effect [9]. Other factors affecting thirst are dry mouth and social influences.

AGING IMPACT ON THIRST:

Healthy persons older than 65 years have shown an age associated impairment in thirst perception. The presence of physical disabilities like blindness, stroke, arthritis limit the elderly from access to fluids, which further confounds the elderly to ingest adequate amount of fluids.

ROLE OF VASOPRESSIN IN WATER HOMEOSTASIS:

Hypothalamus synthesizes arginine vasopressin and it is secreted by neurohypophysis. It is cleared by liver and kidney. Its t½ is about 20 minutes. In persons older than age of 60 years, there is an increase in size of para ventricular and supra optic nuclei of hypothalamus. This suggests that arginine vasopressin secretion increases as persons get old.

REGULATION OF VASOPRESSIN SECRETION:

Hyperosmolality and decreased ECF volume or arterial blood pressure stimulates arginine vasopressin secretion from neurohypophysis [10]. Arginine vasopressin secretion promotes water conservation by the kidney. This corrects hyperosmolality and corrects hypovolemia and arterial pressure. Hypoosmolality decreases arginine vasopressin secretion, which causes water loss and promotes a negative fluid balance and brings back plasma osmolality to normal. Volume expansion has little effect on vasopressin release.

OSMOLALITY:

Circulating vasopressin is undetectable when serum osmolality is less than 280mosm/kg of water in normal individuals. The magnocellular neurons have been found to have intrinsic osmoreceptive properties[11], but several research shows that the most sensitive osmoreceptive cells that are able to sense small changes in plasma osmolality and transduce

these changes into arginine vasopressin secretion are found in the hypothalamus in circumventricular organ called organum vasculosum of the lamina terminalis (OVLT) .The strongest evidence for location of the primary osmoreceptors in this area of the brain are the multiple studies that have demonstrated that destruction of this area disrupts osmotically stimulated arginine vasopressin secretion and thirst without affecting the neurohypophysis or its response to nonosmotic stimuli [12][13]. The osmoreceptors found in hypothalamus are very sensitive to disturbances in plasma osmolality. Even a small change of one percent is sensed by osmoreceptors. This is responsible for the stability of plasma osmolality. Because of these the serum osmolality does not fluctuate more than 1 to 2 percent despite wide variation in water intake. The osmolality threshold for arginine vasopressin ranges from 280 to 290 mosm/kg of water. An increase in serum osmolality of one mOsm/kg of water favours an increase of arginine vasopressin about 0.4 to 1 picogram per millilitre. The response of kidney to arginine vasopressin in circulation is linear. Plasma sodium and other associated anions mainly determine plasma osmolality. Plasma Na^+ is the main trigger for arginine vasopressin secretion. Ineffective osmoles cannot promote vasopressin secretion. Infusion of hypertonic saline or mannitol causes a rise in plasma osmolality .This favours the exit of water from osmoreceptor cells and leads to stimulation of these cells. In the opposite, ineffective osmole like

urea freely move in and out of cell membranes. This does not cause a rise in plasma osmolality. Glucose in normal individuals is an ineffective osmole. In patients with poor control of diabetes mellitus, glucose favours agrinine vasopressin secretion.

ECF VOLUME AND BLOOD PRESSURE:

A ten percent decrease in ECF volume is required to stimulate arginine vasopressin release. When the volume loss is greater it causes an exponential increase in arginine vasopressin in circulation [14]. Hypotension when severe, is a strong stimulant to arginine vasopressin secretion. Loss of blood volume enhances the effect of arginine vasopressin. It overcomes the inhibition of arginine vasopressin secretion caused by hypoosmolality. This concept is most important in hyponatremia associated with states of decreased effective circulatory volume. The hemodynamic influences on arginine vasopressin secretion are mediated partly by neural pathways from baroreceptors located in the atria, aorta, and carotid sinus. Afferent nerve fibers from these receptors rise via the vagus and glossopharyngeal nerves to the nuclei of the tractus solitarius (NTS) in the brainstem [15]. A variety of postsynaptic pathways from the NTS then project via the ventrolateral medulla and the lateral parabrachial nucleus, to the paraventricular and supraoptic nuclei

in the hypothalamus [16]. The pace at which the parasympathetic nerve discharges from baroreceptors in carotid sinus alters the action of vasomotor center located in the medulla. This favours the release of AVP from paraventricular nucleus [17]. Supraoptic nucleus takes part in AVP release caused by disturbances in plasma osmolality. Thus, increased discharge from these nerves in conditions like emesis, chronic liver disease, cardiac failure which are associated with low blood volume favours arginine vasopressin secretion.

OTHER FACTORS REGULATING ARGININE VASOPRESSIN SECRETION:

ORAL FLUID INTAKE:

The peripheral neural sensors also affect the arginine vasopressin secretion in addition to the baroreceptors. Drinking lowers the plasma arginine vasopressin before decreasing plasma osmolality or serum sodium. Arginine vasopressin suppression in response to drinking is influenced by temperature of fluids. Because the suppression is greater when colder fluids are ingested by humans [18]. Sensory afferent originating in the oropharynx and transmission via glossopharyngeal

nerve is the pathway most likely responsible for this arginine vasopressin suppression due to drinking.

NAUSEA:

Nausea appears to be the most prominent non osmotic stimuli to arginine vasopressin secretion. The sensation of nausea, in the absence or presence of emesis, is the strongest stimulus to arginine vasopressin secretion known in humans. A twenty percent rise in osmolality increases arginine vasopressin concentration to 5 to 20 picogram/millilitre. A 20 percent decline in arterial pressure increases arginine vasopressin to 10 to 100 picogram/millilitre. The sense to vomit has been reported to cause arginine vasopressin increase to the level of 200 to 400 picogram/millilitre[19]. This action is mediated by chemoreceptor zone in area postrema in brainstem. Drugs and conditions which cause nausea favours arginine vasopressin release instantaneously and it is extremely potent. Emetic response directs number of pharmacologic and pathologic actions on arginine vasopressin secretion. This is responsible for increase in arginine vasopressin secretion associated with vasovagal reactions, diabetic ketoacidosis, motion sickness and acute hypoxia.

HYPOGLYCEMIA:

Acute hypoglycaemia is also a stimulus for arginine vasopressin secretion. But it is a less potent stimulus when compared to nausea [20]. When glucose is decreased more than 20 percent of normal it can cause the release of arginine vasopressin. The rate at which the glucose level decreases is critical for stimulation of arginine vasopressin release. Because of persistent hypoglycaemia the rise in arginine vasopressin is not sustained [20]. This glucopenic stimuli is of less importance in the physiology or pathology of AVP secretion, because there are probably few drugs or conditions that lower plasma glucose rapidly enough to stimulate release of the hormone, and further this effect is transient.

RENIN ANGIOTENSIN ALDOSTERONE SYSTEM [RAAS]:

The RAAS mediates the regulation of arginine vasopressin secretion [21].Angiotensin II stimulates arginine vasopressin secretion by acting at circumventricular subfornical organ in brain. This is a small anatomical structure found in the posterior aspect of IIIrd ventricle of brain. Because the circumventricular organs are outside the blood brain barrier, the receptors located in subfornical organ can detect even a little increase in angiotensin II levels in plasma [22]. Neural pathways from

subfornical organ reaches the supraoptic and paraventricular nuclei of hypothalamus and mediate arginine vasopressin secretion into circulation [23].

STRESS:

Non specific stress caused by pain, emotion, physical exercise may cause arginine vasopressin secretion.

But it is unknown whether this effect is a direct effect mediated by a specific pathway or secondary to low blood volume or vomiting sensation that is usually associated with vasovagal reactions accelerated by stress. Pain following trauma and surgery stimulates arginine vasopressin release from posterior pituitary. This when combined with post operative hypotonic fluid infusion and water intake promotes water retention and poses the patient at greater risk of dilutional hyponatremia. Arginine vasopressin release in response to pain and temperature is important because painful and febrile illness are associated with osmotically inappropriate secretion of the hormone.

HYPOXIA AND HYPERCAPNIA:

Acute hypoxia and hypercapnia also stimulates arginine vasopressin secretion into the circulation [24] [25]. It is unclear whether

there is a threshold for hypoxia to stimulate arginine vasopressin release. Several studies show that stimulation of arginine vasopressin secretion due to moderate hypoxia (>35 mm of Hg) is not consistent and if arginine vasopressin secretion occurs it seems to be mainly in those who develop nausea or low blood pressure. Severe hypoxia (<35 mm Hg) promotes arginine vasopressin release even without presence of nausea or hypotension. This suggests that there may be hypoxemic threshold for arginine vasopressin secretion. It is responsible for osmotically inappropriate arginine vasopressin release in patients with acute respiratory failure [26]. Hypercapnia also promotes the secretion of arginine vasopressin without the influence of hypoxia and hypotension. It is not known whether this response of arginine vasopressin secretion depends on threshold limit for hypercapnia. Mechanism behind the release of arginine vasopressin due to hypoxia and hypercapnia is unknown, but it may be due to peripheral chemoreceptor and baroreceptor.

DRUGS AND HORMONES:

Some of the drugs and hormones favouring the release of arginine vasopressin are

- Histamine, apomorphine, high doses of morphine,
- Epinephrine , clofibrate, bradykinin,
- Prostaglandin, acetylcholine ,vincristine, 2-deoxyglucose,insulin
- Lithium, naloxone, nicotine, cholecystokinin ,angiotensin II,
- Carbamazepine, , isoproterenol chlorpropamide
- Antidepressants and antipsychotics

Some drugs and hormones inhibiting the arginine vasopressin release are

- Norepinephrine, fluphenazine, haloperidol, promethazine
- Butorphanol, opioid agonists, low doses of morphine,
- Ethanol, carbamazepine, glucocorticoids, clonidine,
- Phenytoin, phencyclidine, muscimol

Vasopressor drugs like noradrenaline supresses AVP secretion indirectly by increasing blood pressure. Excitatory stimulants like cholecystokinin, isoproterenol , nicotine and high doses of morphine act by decreasing arterial pressure and inducing emesis. Carbamazepine suppresses arginine vasopressin release by decreasing osmotic sensitivity.

EFFECTS OF VASOPRESSIN:

Arginine vasopressin actions are expressed by its interaction with 3 different receptors which are coupled with G proteins. The V1a receptor favours the vasoconstrictive and proliferative action in smooth muscle cells of vascular system. It also promotes activation of coagulation by secretion of pro-coagulant factors like factor VIII and von Willebrand's factor from vascular endothelium and exaggerates aggregation of platelets. The V1b receptor confined to anterior pituitary cells, promotes the secretion of adrenocorticotropic hormone from anterior pituitary. Principal cells present in the cortical and medullary collecting duct of kidney contains V2 receptor on the basolateral membrane. This favours the water permeability by an AVP mediated action and permits osmotic equilibrium with interstitium of kidney[27]. Aginine vasopressin interacts with the V2 receptor and produces cyclic AMP by activation of adenyl cyclase. This cyclic AMP, a second messenger starts a series of events that cause insertion of aquaporin-2 channels into the apical side of the principal cells located in collecting duct [28]. Water moves into the cells along the osmotic gradient with the help of this aquaporin-2. Water exits to the systemic circulation across the basolateral membrane rapidly through aquaporin-3. After the decline in arginine vasopressin action, the water channels are returned to the cytoplasm by endocytosis [29].

Arginine vasopressin favours the formation of prostaglandin E_2 and prostacyclin by kidney [30]. This prostaglandin decreases the water conservation and vascular effects of arginine vasopressin. So it prevents an excessive water conservation effect and maintains kidney perfusion [31].

DISTRIBUTION AND CLEARANCE:

Arginine vasopressin concentration is determined by the difference between the rates of secretion from the posterior pituitary gland and removal of the hormone from the vascular compartment via metabolism and urinary clearance. Enzymatic processes by which the liver and kidney inactivate arginine vasopressin involve an initial reduction of the disulfide bridge followed by aminopeptidase cleavage of the bond between amino acid residues 1 and 2. The extent of further degradation and the peptide products that escape into plasma and urine are unknown.

NORMAL AGING AND AVP SYSTEM:

NEUROHYPOPHYSEAL SYSTEM:

There is no degeneration of magnocellular neurons appreciated due to aging. Many studies say that there may be an age associated increase in size of the nucleus producing arginine vasopressin. Thus it

seems that hypothalamic arginine vasopressin neurons do not decrease with age. Infact it may remain stable or increased with age.

ARGININE VASOPRESSIN LEVEL WITH AGING:

In young adults, there exists a diurnal variation of AVP release, with greatest arginine vasopressin release at night. These variations seem to be associated to the sleep-wake pattern and not to the time of the day. The peak in arginine vasopressin release due to sleep is not present in most of the healthy geriatric age group. Low arginine vasopressin and absence of a clear diurnal variation seems to be the cause for frequent micturition during the night in some geriatric population [33]. Many studies suggest that arginine vasopressin concentrations are higher in normal geriatric persons than young adults. There may be an age associated gradual increase in arginine vasopressin levels. Circulating arginine vasopressin correlates with plasma osmolality in young adults but no correlation is seen with geriatric persons[34]. Some studies suggest that there may be gender differences on plasma arginine vasopressin concentration, suggesting a two time higher concentration of arginine vasopressin in elderly man when compared to women. An increase in arginine vasopressin level as the person age is not due to the changes attributable to aging as there is no difference in $t_{1/2}$, distribution

and metabolism of arginine vasopressin in young and elderly persons. So this increased basal plasma arginine vasopressin in elderly is most probably due to central control system managing arginine vasopressin secretion.

ARGININE VASOPRESSIN STIMULATION:

Serum osmolality is identified as the most important stimulant for arginine vasopressin release. Studies say that any osmotic stimulus promotes higher secretion of arginine vasopressin in geriatric persons when compared to young. This indicates that aging results in osmoreceptor hypersensitivity [35]. The ability of intravenous ethanol infusion to suppress the arginine vasopressin secretion has been evaluated in younger and elderly normal persons. Young persons showed a persistent suppression of arginine vasopressin release. But the geriatric population showed an arginine vasopressin suppression at the start of infusion but later showed an elevation in arginine vasopressin to two times that of the baseline. This results shows ethanol is not potent in suppression of arginine vasopressin secretion in geriatric age group and also lost the inhibitory action completely due to ethanol favoured constriction of blood volume [35]. This studies shows, arginine vasopressin responses to osmotic stimulus is high due to osmoreceptor

hypersensitivity. Arginine vasopressin secretion to erect posture is decreased due to impairment in baroreceptor function.signals from the baroreceptor to the osmoreceptor is suppressive. A defect in this would lead to an inappropriate production of arginine vasopressin. This defects along with changes in kidney function due to aging, places the geriatric persons at risk of hyponatremia.

INTEGRATION OF ARGININE VASOPRESSIN SECRETION AND THIRST:

In normal physiologic circumstances, the sensitivity of the osmoregulatory system for AVP secretion is responsible for maintenance of plasma osmolality within narrow limits by adjusting amount of water excreted through the kidneys following small changes in osmolality. Stimulated thirst does not represent a major regulatory mechanism under these conditions, and an unregulated fluid ingestion supplies water in excess of true need. This is then excreted in relation to osmoregulated pituitary arginine vasopressin secretion. However, when unregulated water intake is not enough to supply body needs in the presence of plasma arginine vasopressin levels sufficient to produce maximal antidiuresis, then serum osmolality rises to levels that trigger thirst leading to water intake in proportion to the increase in osmolality above this thirst threshold. Thirst essentially represents a back-up mechanism

that comes into play when pituitary and renal mechanisms prove inadequate to maintain plasma osmolality within a few percent of basal levels. Stimulation of arginine vasopressin secretion at serum osmolalities below the threshold for subjective thirst acts to maintain an excess of body water adequate to eliminate the need to consume water whenever minimal elevations in serum osmolality occur. This system of different effective thresholds for thirst and arginine vasopressin secretion complements many studies that have demonstrated excess unregulated drinking in both humans and other animals. Only when this mechanism becomes insufficient to maintain body fluid homeostasis, thirst-induced regulated fluid intake becomes the predominant mechanism to prevent severe dehydration.

THE KIDNEY AND WATER BALANCE:

Regulation of water balance largely depends on the kidney's ability to excrete urine with an osmolality that varies from a minimum value of 50 mosm/kg water to a maximum of 900 to 1400 mosm/kg water. This wide range of urine osmolality indicates the changes in collecting duct water permeability depending on the absence of AVP (low urine osmolality, production of dilute urine, water diuresis) or the presence of AVP (high urine osmolality, production of concentrated urine, antidiuresis).

The kidney's ability to produce maximal urine dilution in states of water excess depends on 3 important steps:

1. Adequate delivery of filtrate to the collecting tubule thereby ensuring sufficiently high flow rates that prevent the equilibration of urine in the collecting duct with the hypertonic renal interstitium. Adequate distal delivery requires a normal GFR and normal reabsorption in the proximal segment.
2. Active transport of sodium chloride without water in the thick ascending limb of the loop of Henle. This decreases the osmolality of fluid reaching the distal tubule to 50 to 100 mosm /kg of water.
3. Absence of vasopressin. This maintains the intrinsic property of low water permeability of the collecting duct.

The capacity of the kidney to produce maximum urine concentration and reduce water loss to a minimum in a water depleted state requires the following important steps:

1. Active transport of NaCl without water in the thick ascending limb of the loop of Henle. This produces dilution of the fluid in the tubular lumen and concentration in the renal interstitium.
2. Enhancement of the effect of above said step by the entry of NaCl into the descending limb of the loop of Henle and the efflux of

water from this segment (through water permeable channels known as aquaporin-1) thereby progressively increasing the osmolality both of the fluid in the lumen of the descending limb of the loop of Henle and the renal interstitium from the corticomedullary junction to the inner medulla. This process is known as countercurrent multiplication.[36].

3. Maintenance of the corticomedullary osmotic gradient by the vasa recta that reach osmotic equilibrium with the interstitium, as they allow solutes and water to pass through and remove fluid from the renal interstitium (ascending vasa recta blood flow is almost double that of descending vasa recta) [37].This process is known as countercurrent exchange.
4. Preservation of a relatively low blood flow in the renal medulla and papilla that prevents the removal of solutes (largely NaCl and urea) from the renal interstitium and
5. Presence of vasopressin to ensure water reabsorption from the collecting duct.

EFFECT OF AGING IN KIDNEY:

CHANGES IN STRUCTURE AND FUNCTION:

Aging is accompanied by changes in the anatomy and function of the kidney. The total glomeruli number in nephron decreases by 30% to

40% with increasing age and the percentage of hyalinized or sclerotic glomeruli increase by 10% to 30%. This phenomenon accelerates after 40 years of age, causing the residual glomeruli also to undergo changes. Thus, there is a decrease in effective filtering surface and no of epithelial cells, with an increase in the number of mesangial cells and thickening of the glomerular basement membrane. Normal aging process also produces changes in the renal vasculature that leads to obliteration of the arteriolar lumen and loss of the glomerular capillary tuft which take place primarily in the cortical glomeruli. Renal blood flow declines with age at the rate of around 10% with every decade after young adulthood so that by 90 years of age the renal plasma flow is approximately 300 ml/min—a value that is only 50% of the RPF found at 30 years of age. Glomerular filtration rate (GFR) remains relatively constant until age of 40 years, after which it declines at an annual rate of approximately 0.8 mL/min/1.73 m2.

CHANGES IN WATER REGULATION:

RENAL WATER RETENTION:

The aging kidney exhibits impairment in the ability to dilute the urine and excrete a water load. The most important factor for decline in diluting capacity of aging kidney is the age related decrease in RPF and GFR. In addition to impaired diluting capacity, the decrease in renal plasma flow and GFR favours the passive reabsorption of fluid which increases the risk of fluid overload and hyponatremia. This effect is

clinically evident in elderly patients who have congestive heart failure, extracellular volume depletion and hypoalbuminemia. Diuretics, (thiazides especially) can reduce the diluting capacity of the kidney. In the elderly, this effect becomes significant when it is superimposed on the already diminished diluting capacity of the kidney, thereby increasing the risk of developing water intoxication by impairing the ability to excrete excess water.

RENAL WATER LOSS:

It is known that there is an age associated decline in renal concentrating ability. An age-related increase in vasopressin secretion may result in down-regulation of AVP receptors in the kidney which maybe the basis for decreased renal concentrating capacity in the elderly.

SODIUM REGULATORY CAPACITY:

RENAL SODIUM RETENTION:

A number of factors and circumstances may lead to Na retention. There is increased sodium conservation owing to age related decrease in renal blood flow and GFR. Conditions like congestive heart failure, cirrhosis, nephrotic syndrome that lead to secondary hyperaldosteronism is common in elderly. Drugs like NSAIDS used commonly in elderly may augment sodium retention..

RENAL SODIUM LOSS:

When compared with young individuals elderly individuals have an exaggerated sodium loss in urine after a water load. Benign hypertension patients have excess sodium excretion with increasing age. Mechanisms underlying this tendency maybe due to a number of factors and are related to the effects of senility of atrial natriuretic hormone, the RAAS and renal tubular function.

AGE RELATED CHANGES IN SECRETION, REGULATION AND ACTION OF ATRIAL NATRIURETIC HORMONE:

Atrial natriuretic hormone is produced, stored and secreted in atria of the heart. It produces natriuresis & dieuresis by its effect on kidney. It acts on the blood vessels producing vasodilation thereby decreasing the blood pressure. It may be an important factor associated with altered renal sodium handling due to aging. In a comparison of normal young men with elderly men in nursing homes, a fivefold increase in mean basal ANH levels with an exaggerated ANH was noted in the elderly in response to saline infusion. In response to the stimulus of head-out water immersion, ANH levels of healthy older individuals (age 62–73 years), which were twice as high at baseline as in young subjects (age 21–28 years), rose to a greater extent than in the young [38]. Thus increase in age results in increase in basal levels of ANH and an increase in response

to both physiologic and pharmacologic stimuli. This may be the consequence of age related decrease in cardiac muscle compliance. Studies suggest that the action of ANH on the kidney may be higher in geriatric age group than in young persons. It is known that ANH can interact with RAAS. Increase in ANH results in downregulation of renin release, plasma renin function, angiotensin II and aldosterone levels, suggesting an indirect negative regulation of aldosterone secretion by atrial natriuretic hormone. Thus, atrial natriuretic hormone may cause urinary Na+ excretion in 2ways by inhibiting aldosterone secretion and by direct natriuretic action. Atrial natriuretic hormone may be a significant cause of age related urinary Na+ excretion. This phenomenon may be the result of rise in baseline atrial natriuretic hormone levels, augmented ANH reaction to stimuli, increase in the response of the kidney to atrial natriuretic hormone, and atrial natriuretic peptide induced downregulation of adrenal sodium-retaining hormones.

CHANGES IN RAAS WITH AGE:

Studies suggest that aging affects the RAAS. Normal elderly (age 61–70 years) with normal dietary sodium intake have lower serum renin function and aldosterone levels while in the supine posture than normal young adults (age 21–30 years). On changing to upright posture and

during Na+ depletion, prominent rise in levels of renin and aldosterone occurred in the young and elderly, but average values reached were always lower in the older age group [39]. The fall in serum renin function in the older population is not due to changes in serum renin substrate levels but due to fall in active renin levels. It may be caused by reduced activation of renin. The reduction in serum renin activity may also be due to inhibition by elevated levels of atrial natriuretic hormone on renin release. Fall in aldosterone levels with age seems to be due to reduction in serum renin function due to age and not to age related changes in the adrenals. It is probable that the reduction in aldosterone levels leads to urinary salt loss in the geriatric age group. Alterations in intrinsic tubular function may also play a role in salt loss. Faulty sodium reabsorption has been noted along with reduced response of renal tubule to aldosterone administration. The reduction in activity of the RAAS may be the result of changes in K+ regulation. Hyporeninemic hypoaldosteronism occurs most frequently in geriatric individuals, particularly diabetics. The hyperkalemia which is a feature of the disorder gets corrected on mineralocorticoid administration and maybe the effect of interplay between chronic renal disease & the hormonal changes of aging. The risk of ACE inhibitors leading to hyperkalemia is particularly high in older people, and may also be a result of interaction between effect of the drug and physiologic alteration caused by aging.

ETIOLOGY OF HYPONATREMIA:

The plasma Na+ sodium level is determined by the body's content of sodium, potassium, and TBW. Thus:

Serum sodium: Total body Na^+ + total body K^+ / total body water.

Hyponatremia can therefore occur by an increase in TBW, a decrease in body solutes (either Na^+ or K^+), or any combination of these. But in most cases more than one mechanism is responsible for hyponatremia. In approaching the hyponatremic patient, it is very important to ensure that hyponatremia reflects a hypo-osmotic state and is not a consequence of the causes of pseudohyponatremia. Assessment of ECF volume provides a useful working classification of hyponatremia as it can be associated with decreased, normal, or high total body sodium:

(1) Hyponatremia with ECF volume depletion,

(2) Hyponatremia with excess ECF volume, and

(3) Hyponatremia with normal ECF volume [40].

HYPONATREMIA WITH EXTRACELLULAR FLUID VOLUME DEPLETION:

Patients with hyponatremia who have ECF volume depletion have reduced total body Na^+ and TBW. But the deficit in total body Na^+ is in excess of deficit in total body water. Volume depletion can be associated with normal supine BP but fall of the systolic level greater than 15 mm Hg on standing. Also, a rise in heart rate of more than 15beats/min on standing from supine posture and reduced JVP can be noted. A severe volume loss can lead to fall in BP in lying posture also, fall in tissue plasma flow, and reduced skin turgor. Ocular pressure falls and mucous membranes become dry. Signs of intracellular volume loss come to play only when the volume depletion is quite acute or severe, as retention of H_2O can compensate the severity of the fluid depletion. A rise in serum creatinine and a proportionately greater rise in BUN concentration are characteristically seen indicating the associated fall in glomerular filtration rate and accentuated urea reabsorption by the kidney If sufficiently severe, volume depletion is a potent stimulus to AVP release. When the osmoreceptor and volume receptor receive opposing stimuli, the former remains fully active but the set-point of the system is lowered. Thus, in the presence of hypovolemia, AVP is secreted and water is retained despite hypo-osmolality. Whereas the hyponatremia in this

setting clearly involves a depletion of body solutes, a concomitant failure to excrete water is critical to the process. In hypovolemic hyponatremia the source of fluid loss is whether renal or extrarenal in origin is assessed by examining the urinary sodium concentration.

EXTRARENAL LOSS:

A urinary sodium concentration of ≤ 20 mEq/L reflects an adequate response of kidney to volume loss and indicates another source of fluid loss apart from the kidneys. This is most commonly seen in patients with gastrointestinal disease with vomiting or diarrhea. Other causes of extrarenal loss include loss of fluid into the third space, such as the abdominal cavity in pancreatitis or the bowel lumen with ileus. Burns and muscle trauma can also leads to large fluid and electrolyte losses. Because many of these pathologic states are associated with thirst, an increase in either orally or parenterally taken free water leads to hyponatremia.

RENAL LOSS:

Hypovolemic hyponatremia in patients with urinary Na^+ concentration is ≥ 20 mEq/L renal loss of fluid volume.

DIURETICS:

Diuretic-induced hyponatremia accounts for a significant proportion of symptomatic hyponatremia in hospitalized patients. It occurs almost exclusively with thiazide rather than loop diuretics, most likely because the former have no action on urine concentrating function in contrast to the latter. The hyponatremia is normally seen within 14 days but can occur up to 2 years in most patients [41]. Underweight women appear to be particularly prone to this complication [42] and advanced age has been found to be a risk factor in some patients. Studies on diluting capacity of geriatric patients shows that thiazide diuretics aggravate the already slower recovery from hyponatremia induced by water ingestion in this population [43].

Diuretics can cause hyponatremia by a variety of mechanisms:

(1) Volume depletion, which results in impaired water excretion by both enhanced AVP release and decreased volume delivery to the diluting segment;

(2) Direct effect of diuretics on the diluting segment; and

(3) K^+ depletion causing a decrease in the water permeability of the collecting duct as well as an increase in water intake

K^+ depletion leads to hyponatremia independent of the Na^+ depletion that frequently accompanies diuretic use [43]. The concomitant administration of K^+-sparing diuretics does not prevent the development of hyponatremia. Diagnosis of diuretic induced hyponatremia is suspected when there is other electrolyte abnormalities as well as high urinary chloride clearance.

SALT LOSING NEPHROPATHY:

In advanced renal insufficiency some patients may have salt losing nephropathy. Salt-wasting nephropathy refers to a state of volume loss and associated fall of serum Na^+ levels observed in patients with advanced CRF (GFR less than15 millilitres/minute) consuming diet with low Na^+ content. In the majority of these patients, the Na^+-wasting tendency is not one that manifests itself at normal rates of sodium intake; however, some patients with interstitial nephritis, MCD, ADPKD with sufficient Na^+ wasting exhibit hypovolemic hyponatremia [44].

BICARBONATURIA:

Sodium and water excretion are also increased when a non reabsorbable anion appears in the urine .Patients with proximal renal tubular acidosis exhibit renal sodium and potassium wasting despite modest renal insufficiency because bicarbonaturia present in the renal

tubular acidosis obligates these cation losses. The metabolic alkalosis and bicarbonaturia that accompany severe vomiting or nasogastric suction is also associated with sodium loss. In these patients, for the maintenance of electroneutrality, the excretion of HCO_3^- requires the excretion of cations, including sodium and potassium. Whereas the renal losses in these clinical settings may be hypotonic, the volume contraction-stimulated thirst and water intake can result in the development of hyponatremia.

MINERALOCORTICOID DEFICIENCY:

It has been recognized that adrenal insufficiency is associated with impaired renal water excretion and hyponatremia. This diagnosis of adrenal insufficiency should be considered in the volume-contracted hyponatremic patients whose urinary Na^+ concentration is high, particularly when the serum K^+, BUN, and creatinine levels are elevated. The mechanism of the defect in water excretion associated with mineralocorticoid deficiency is mediated by AVP and by AVP-independent intrarenal factors, both of which are activated by depletion of ECF volume.

KETONURIA:

The presence in the urine of an osmotically active nonreabsorbable solute causes renal excretion of sodium and culminates in volume depletion. Glycosuria secondary to uncontrolled diabetes mellitus, mannitol infusion, or urea diuresis after relief of obstruction is a common setting for this disorder. In patients with diabetes, the Na^+ wasting caused by the glycosuria can be aggravated by ketonuria because hydroxybutyrate and acetoacetate also cause urinary electrolyte losses. Ketonuria can contribute to the renal sodium wasting and hyponatremia seen in starvation and alcoholic ketoacidosis.

CEREBRAL SALT WASTING SYNDROME:

Cerebral salt wasting is manifested by hyponatraemia, urinary loss of NaCl, and fluid loss in persons having neurological disorders [45]. This syndrome of unclear pathogenesis is seen frequently in head injury patients with SAH. It normally gets corrected in a couple of weeks. The mechanism of urinary sodium excretion has been ascribed to a BNP or reduced sympathetic activity.

HYPONATREMIA WITH EXCESS EXTRACELLULAR FLUID VOLUME:

Patients with hypervolemic hyponatremia show an increase in plasma Na^+ followed by a proportionately larger increase in TBW, resulting in a decreased serum Na^+ levels. In hypervolemic hyponatremia the source of fluid loss is whether renal or extrarenal in origin is assessed by examining the urinary sodium concentration. Arterial filling and circulatory integrity is decreased in CCF, chronic liver disease, and nephrotic syndrome. This can lead to fall in serum sodium levels because of increased AVP release [46]. This effect is directed via carotid baroreceptors that sense a fall in arterial stretch and override the suppressive action of hypotonicity on arginine vasopressin secretion. In conditions other than kidney failure, these conditions show prominent sodium retention (urinary sodium levels less than 10 mEq/Litre). This retention may be hidden by the concurrent usage of diuretics, which are frequently used in treating these patients. These agents can further contribute to the abnormal water excretion seen in these states. The degree of hyponatremia provides an indirect index of the associated neurohumoral activation and is an important prognostic indicator in hypervolemic hyponatremia.

EXTRA RENAL CAUSES:

A urinary sodium concentration of less than 20 mEq/L points to a extra renal cause of hypervolemic hyponatremia.

CONGESTIVE CARDIAC FAILURE:

Reduced perfusion caused by decrease in ejection fraction in patients with CCF leads to stimulation of RAAS, ADH, noradrenaline that leads to faulty H_2O excretion by the kidneys and causes hypotonic hyponatremia. Hyponatremia is common in patients with severe CCF in whom a plasma sodium $\leq$ 130 mEq/Litre indicates a reduced life expectancy unless heart function improves [47]. A combination to H_2O restriction, an ACE inhibitor, and a loop diuretic helps to normalize the hyponatremia [48].

CIRRHOSIS:

There is no disturbance in kidney water handling in the earlier course of the disease before the onset of ascites. Persons having end stage liver disease frequently manifest hyponatremia due to their inability to excrete a water load [49].With the progression of liver disease the secretion of AVP increases. This predisposes the patient with cirrhosis to hyponatremia [50]. In advanced cirrhosis due to marked dilation of blood vessels in splanchnic circulation and stimulation of the RAAS and

adrenergic nerves, there is reduction in renal blood flow. This also appears to contribute to a smaller extent to faulty urinary H_2O loss. The chances of manifesting hyponatremia is more in patients with cirrhosis who are alcoholic (beer potomania) or in persons having fluid loss as a result of diuretic use or ascitic fluid tap without edema. A plasma sodium ≤ 130 mEq/litre has bad outcome and levels <125 mEq/litre are seen in advanced cirrhosis. Commonly cirrhotics have asymptomatic hyponatremia though it may aggravate hepatic encephalopathy [51].

NEPHROTIC SYNDROME:

Faulty urinary water loss and mild hyponatremia is seen in persons having nephrotic syndrome .The prevalence of hyponatremia in the nephrotic syndrome is lesser than CCF or cirrhosis. It is most likely due to the higher blood pressure, higher GFR, and more modest impairment in Na^+ and water excretion in nephrotic syndrome than in congestive heart failure or cirrhosis [52]. The pathogenesis may vary in patients with normal kidney function like minimal change disease than in persons having reduced GFR. ADH secretion stimulated by a reduction in blood volume seems to be impaired in persons with nephrotic syndrome, albumin deficiency & normal kidney function. In contrast, hypervolemia may be more prevalent in patients with underlying glomerular pathology and reduced renal function. Rigorous diuretic usage may lead to severe sodium loss in nephrotics.

RENAL FAILURE:

Hyponatremia can occur with end stage kidney failure. In such people with renal failure the excretion of free water is limited by a decrease in GFR. In later stages of impairment in renal function, the urine osmolality ranges from 200 to 250 milliosmoles/kilogram of water inspite of appropriate downregulation of AVP release. Thus unlimited fluid consumption may cause hyponatraemia. A decrease in GFR with an increase in thirst underlies the hyponatremia of patients with renal insufficiency. The higher level of urine osmolality is a result of increase in loss of solutes per nephron causing osmotic diuresis. Persons having ESRD, on hemodialysis experience significant collection of extracellular fluid during interdialysis times, but the fall in Na^+ is rarely severe which is because the water intake is an effect of hypertonicity due to salt ingestion.

HYPONATREMIA WITH NORMAL ECF VOLUME:

HYPOTHYROIDISM:

Patients with severe hypothyroidism may have hyponatremia with normal ECF volume. There may be decrease in GFR and decrease in renal plasma flow in patients with hypothyroidism. There is an alteration in the osmotic threshold of arginine vasopressin secretion. Patients with severe hypothyroidism have higher levels of AVP. There is also a

decrease in glomerular filterate delivery to the diluting segment of kidney. Thus both these mechanism operate in patients with hypothyroidism and contributes to hyponatremia by impaired water excretion.

GLUCOCORTICOID DEFICIENCY:

Glucocorticoids may exert direct inhibitory action on AVP secretion. So its deficiency increases vasopressin secretion in patients with primary adrenal insufficiency [53]. Prolonged glucocorticoid deficiency is associated with decrease in renal hemodynamics that impairs water excretion. Elevated serum K^+ is specifically not seen in isolated glucocorticoid deficiency but frequently found in other forms of adrenal deficiency. It is an important clue in differentiating different forms adrenal insufficiency.

SYNDROME OF INAPPROPRIATE ANTI DIURETIC HORMONE SECRETION:

In these patients, the AVP secretion is not controlled by hemodynamic or osmotic stimulus. This leads to water retention. Control of sodium balance remains stable in patients with SIADH. Urinary sodium concentration reflects sodium intake in these patients. Urinary

Na^+ concentration is usually high, but it is low in SIADH patients with low sodium diet. Thus the ECF volume appears normal and patients are without signs of hypervolemia. The diagnosis of SIADH depends on

1. The detection of hypoosmolar hyponatremia ,
2. Inappropriate urine concentration (osmolality more than 100 milliOsmoles/kg of water),
3. Euvolaemia that is clinically evident,
4. High urine Na^+ levels with normal sodium consumption,
5. Normal GFR and
6. Absence of diuretic use, glucocorticoid insufficiency, or hypothyroidism

Accurate diagnosis of SIADH may need measurement of plasma ADH, and the effect of a water load test in some patients. Results indicative of diagnosis of SIADH are:

1. increased AVP despite low plasma osmolality,
2. failure to lower urine osmolality < 100 milliosmoles/kg water in response to a water load
3. Inability to excrete at least eighty per cent of the load within 4 hours, and

4. Inability to normalize the low sodium values with volume expansion but improvement after water restriction.

CAUSES OF SIADH:

There are many causes of SIADH including

- Tumors of the lung , gastrointestinal tract, urological malignancies, sarcomas,
- Various acute or chronic infections of the respiratory system,
- Various central nervous system disorders including infections, delirium, multiple sclerosis, shy dragger syndrome, acute intermittent porphyria, and cerebrovascular accidents including intracerebral bleed.
- There are number of drugs causing SIADH some of which are fluoxetine , carbamazepine, nicotine, oxytocin, tricyclic antidepressants, desmopressin, vasopressin analogues, vincristine and antipsychotic drugs.

OTHER CAUSES OF HYPONATREMIA

Postoperative hyponatremia:

Postoperative hyponatremia develops due to persistent vasopressin secretion in patients treated with large amounts of electrolyte-free water. Associated stressors like pain,nausea and drugs trigger vasopressin release. However many patients are euvolaemic and asymptomatic.

Hyponatraemia caused by decreased excretion of solutes

Low solute excretion decreases the maximal urine volume and causes dilutional hyponatraemia if associated with a high water intake. Examples are the tea-and-toast diet, in aged individuals of poor means, and beer potomania where there is decreased solute excretion.

Primary polydipsia

Primary polydipsia is seen in psychotics mainly schizophrenics, and in anxious, middle-aged females. These people drink a large amount of water that is compounded by a diminished capacity of renal water excretion. Contributing factors include a central defect in thirst regulation , an excessive ADH secretion and consequences of drug therapy.

Primary polydipsia also occurs in lesions affecting hypothalamic thirst centre as in sarcoidosis, multiple sclerosis and tuberculous meningitis. The recreational drugs like amphetamine and ecstasy cause hyponatraemia by increasing water intake and ADH release.

Hyponatremia associated with sodium-free irrigant solutions

Sodium-free flushing solutions with glycine, sorbitol, or mannitol are used in TURP and gynaecological surgeries. The solutions have low osmolality that decrease serum sodium. These organic solutes undergo metabolic degradation leaving behind the free water of the irrigant solution. The diagnosis is made from the clinical history and by the demonstration of a high osmolal gap.

Other causes of hyponatremia due to excessive water intake

Multiple tap water enemas in thin subjects

Accidental intake of large amounts of water during swimming

MATERIALS AND METHODS

STUDY CENTRE:

RG GGH AND MMC, Chennai

ETHICAL COMMITTEE APPROVAL:

Ethical committee clearance obtained from Institutional Ethical Committee of MADRAS MEDICAL COLLEGE held on 19.06.2012

STUDY DESIGN:

Hospital based observational study.

PERIOD OF STUDY:

6 months, from June 2012 to December 2012

STUDY POPULATION:

Hundred patients.

INCLUSION CRITERIA:

1. Elderly patients 65 years and above.
2. Patients with serum sodium levels less than 135 mEq/litre.

EXCLUSION CRITERIA:

1. Patients with age less than 65 years.
2. Pseudohyponatremia.

DETAILS OF THE STUDY:

100 patients admitted in RGGG Hospital having serum sodium level less than 135 mEq/litre are included in the study with proper informed consent in their regional language. Detailed history and clinical examination were performed in patients diagnosed to have hyponatremia. Blood and urine samples were taken from patients for relevant investigations with proper consent.

SERUM SODIUM:

Sodium is the principal cation in extracellular fluid. It is essential for the proper control of blood volume, blood pressure, osmotic equilibrium and pH. It is measured by taking 5 ml of venous blood. Serum sodium level is estimated using ion specific electrode in the automated analyzer which performs various analysis within a single machine.

PLASMA OSMOLALITY:

Plasma osmolality is defined as the measure of concentration of solutes in one kilogram of water. It is expressed in milliosmoles/ kg of water.

It can be estimated by the following formula:

Plasma osmolality = 2x serum [Na^+] + glucose/18+BUN/2.8

- Serum sodium in milliequivalents/litre
- Random blood glucose in milligrams/decilitre
- BLOOD UREA NITROGEN in milligrams/decilitre

Normal serum osmolality is 275 to 290 mOsm/kg of water.

ASSESSMENT OF VOLUME STATUS:

By the assessment of volume status patients with hyponatremia were categorized into euvolemic, hypovolemic and hypervolemic. It is assessed clinically by examining for

- Pulse
- Blood pressure
- Examining mucus membranes
- Urine output
- Jugular venous pressure
- Hepatojugular reflex
- Presence or absence of cold and clammy extremities
- Peripheral edema

- Ascites
- Pulmonary congestion
- Capillary refill.

URINARY SODIUM ESTIMATION:

Patients after the assessment of volume status is estimated for the urinary sodium excretion by urine spot sodium examination test. When urinary sodium excretion is more than 20 it points to sodium loss attributable to a renal cause and when it is less than 20 it points to extrarenal source of sodium loss.

THYROID FUNCTION TEST:

This test is performed in selected patients to rule out hypothyroidism in euvolemic hyponatremia. Estimation of TSH is the most sensitive test to detect hypothyroidism. The normal range of the TSH in our laboratory is between 0.3 to 5.0 mIU/litre.

COSYNTROPIN TEST:

It is done in selected patients with euvolemic hyponatremia. It is a stimulation test performed to rule out the adrenal insufficiency. In this test 250 microgram of synthetic ACTH co syntropin is injected intravenously or intramuscularly whichever is feasible. Basal levels of ACTH and cortisol are measured before injection. Patient should be

prepared by overnight fasting. Venous blood is collected at thirty minutes and sixty minutes after the injection and the values are interpreted to rule out adrenal insufficiency.

OBSERVATION AND RESULTS

TABLE 1: AGE DISTRIBUTION

AGE	NO OF PATIENTS	PERCENTAGE
65-75	72	72
76-85	23	23
86-95	5	5

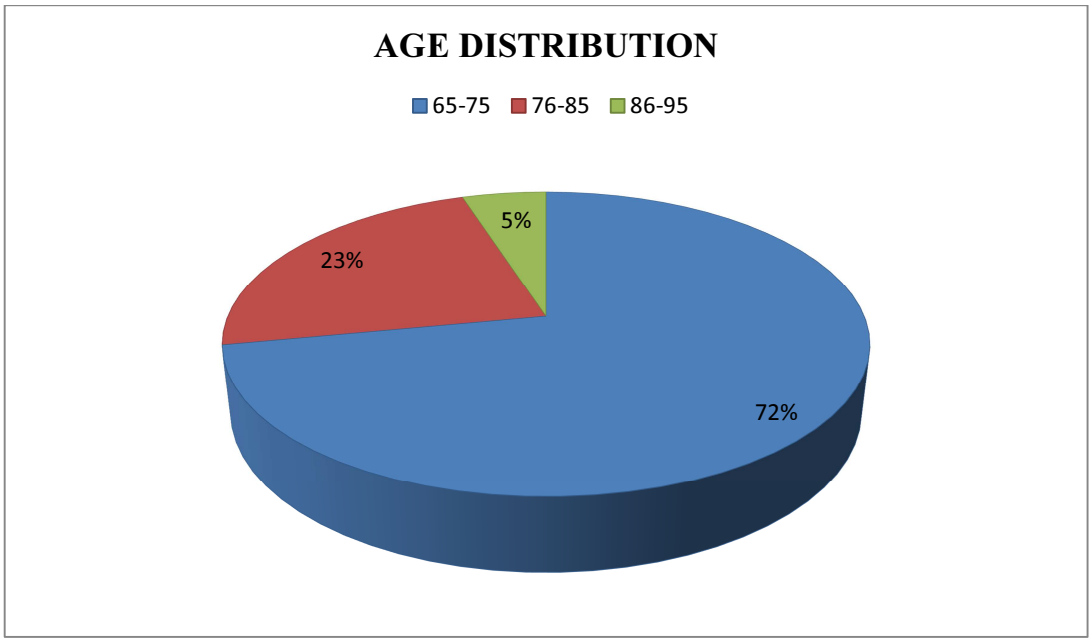

FIGURE 1 AGE DISTRIBUTION

AGE DISTRIBUTION:

Out of hundred patients studied, 72 patients (72 percent) fall within the age group of 65 to 75 years, 23 patients fall within the age group of 76 to 85 years (23 percent), and 5 patients fall within the age group of 86 to 95 years.

TABLE 2: SEX DISTRIBUTION

SEX	NO.OF PATIENTS	PERCENTAGE
MALE	57	57
FEMALE	43	43

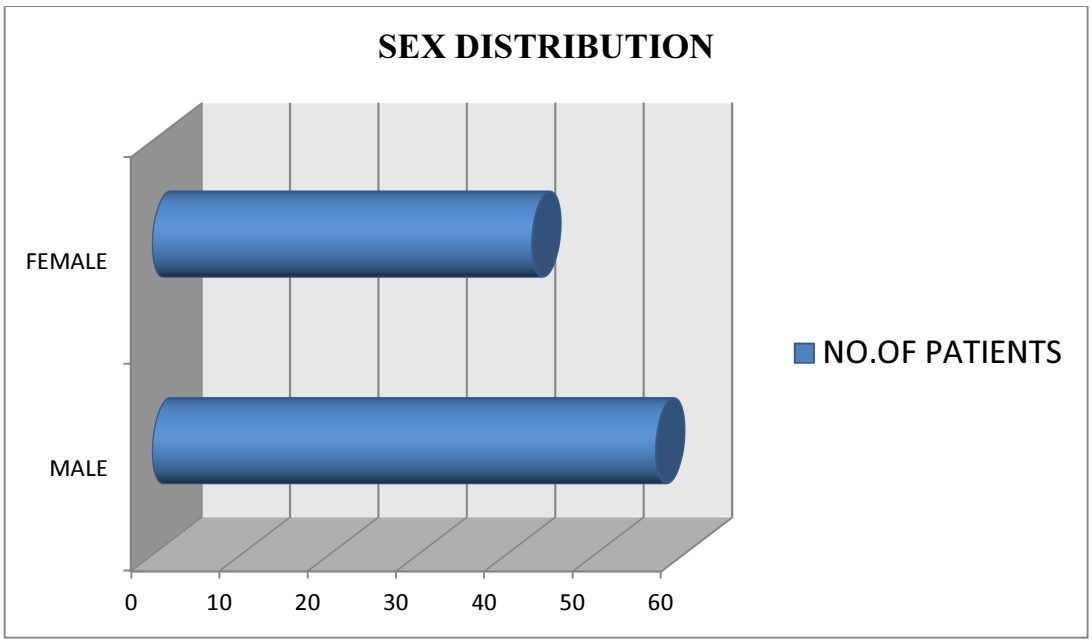

FIGURE 2 SEX DISTRIBUTION

SEX DISTRIBUTION:

Out of 100 patients studied, 57 were male patients (57 percent) and 43 were female patients (43 percent).

TABLE 3: SEX DISTRIBUTION IN DIFFERENT AGE GROUP

AGE	NO.OF PATIENTS	MALE	PERCENTAGE OF MALE	FEMALE	PERCENTAGE OF FEMALE
65-75	72	42	73.68	30	69.76
76-85	23	11	19.29	12	27.9
86-95	5	4	7.01	1	2.32

Out of 72 patients in the age group of 65 to 75, 42 patients were male (73.68 percent), 30 patients were female (69.76 percent).In the age group of 76 to 85 years, out of 23 patients, 11 were male patients (19.29 percent), 12 were female patients (27.9 percent).Out of 5 patients in the age group 0f 86 to 95, 4 patients were male (7.01 percent) and 1 patient was female (2.32 percent).

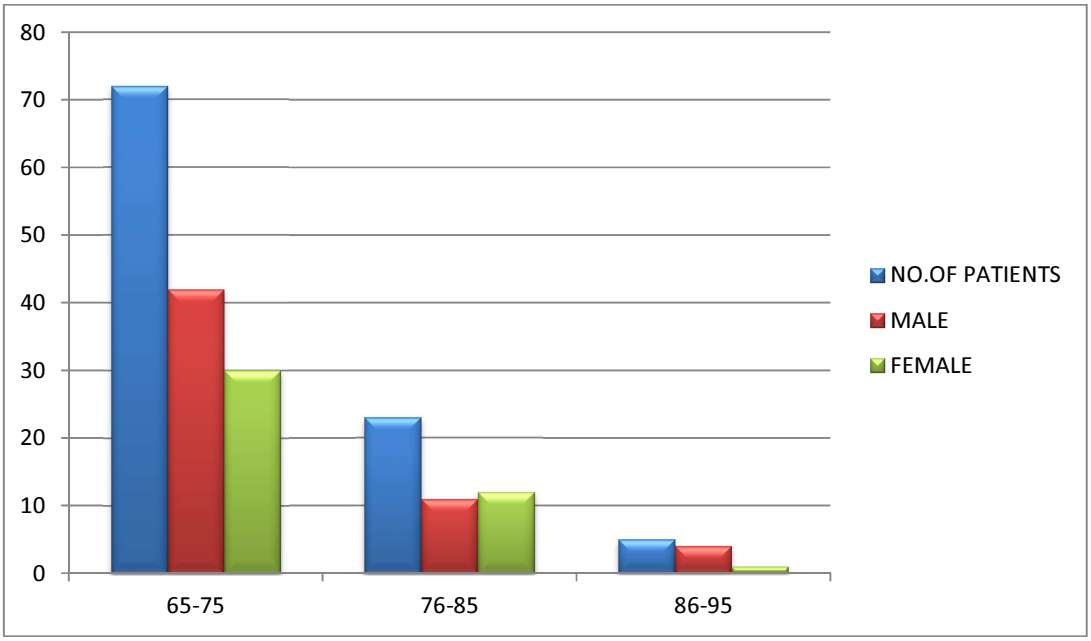

FIGURE 3 SEX DISTRIBUTION IN DIFFERENT AGE GROUP

TABLE 4: COMORBID ILLNESS IN HYPONATREMICS

COMORBIDITY	NO.OF PATIENTS
HYPERTENSION	52
DIABETES MELLITUS	28
CAD	18
TB	3
HYPOTHYROIDISM	4
CKD	11

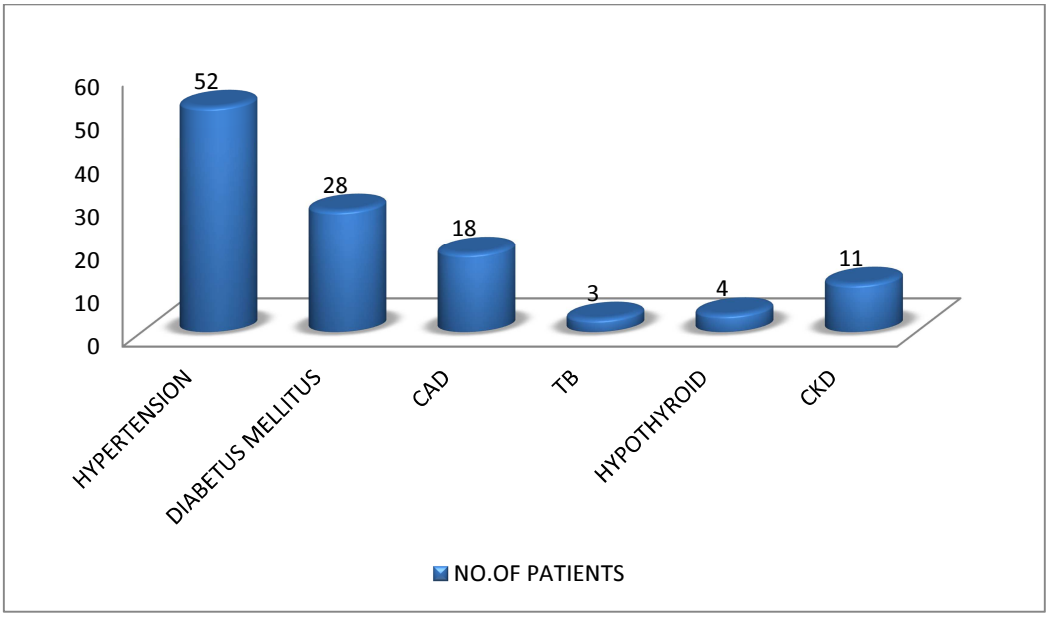

FIGURE 4 COMORBID ILLNESSES IN HYPONATREMICS

COMORBID ILLNESS IN HYPONATREMIC PATIENTS:

Out of 100 patients, 52 patients had hypertension, 28 patients had Diabetes mellitus, 18 patients had CAD, 3 patients had TB, 4 patients had hypothyroidism, and 11 patients had CKD.

TABLE 5: COMORBID ILLNESS IN MALES

COMORBIDITY	NO.OF PATIENTS
HYPERTENSION	32
DIABETES MELLITUS	15
CAD	12
TB	2
CKD	5

COMORBID ILLNESS IN MALES:

Out of 57 male patients, 32 had hypertension, 15 had diabetes mellitus, 12 had CAD, 2 had TB and 5 had CKD.

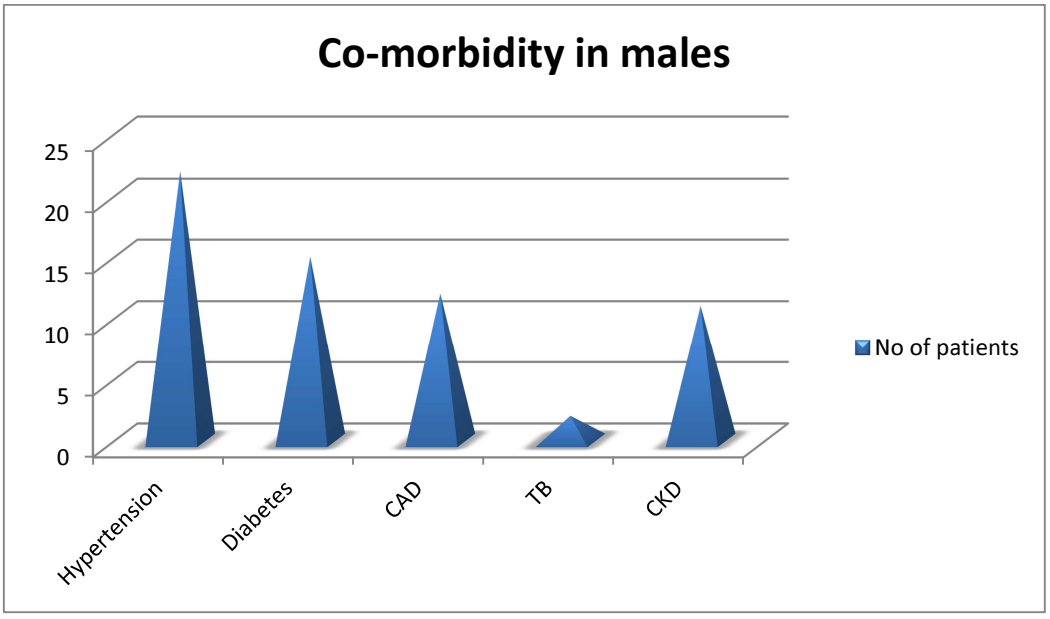

Figure 5: Comorbid illness in males

TABLE 6: COMORBID ILLNESS IN FEMALES

COMORBIDITY	NO OF PATIENTS
Hypertension	20
Diabetes	13
CAD	6
TB	1
Hypothyroidism	4
CKD	6

COMORBID ILLNESS IN FEMALES:

Out of 43 female patients, 20 had hypertension, 13 had diabetes mellitus, 6 had CAD, 1 had TB, 4 had hypothyroidism, 6 had CKD.

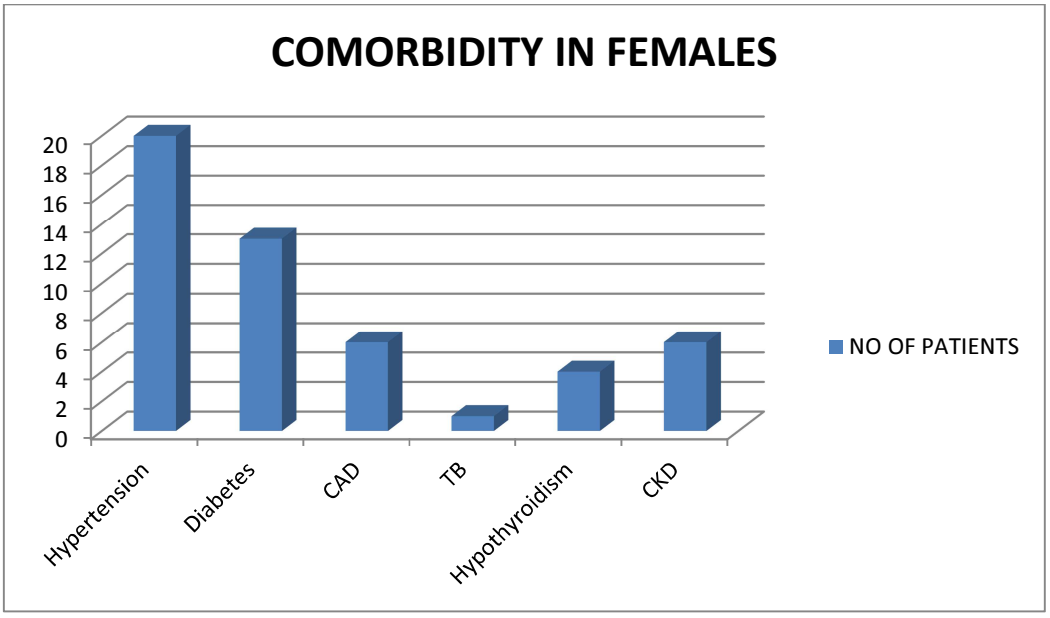

FIGURE 6

TABLE7: SYMPTOMS IN HYPONATREMIC PATIENTS

SYMPTOMS	NO OF PATIENTS
Malaise	92
Nausea	52
Altered sensorium	51
Headache	28
Vomiting	26
Diarrhea	7
Seizures	9
Coma	6
Cramps	9

SYMPTOMS IN HYPONATREMIC PATIENS:

Out of 100 patients, 28 patients had headache, 52 patients had nausea, 26 had vomiting, 7 had diarrhea, 92 had malaise, 51 had altered sensorium, 9 had seizures, 6 had coma and 9 had cramps.

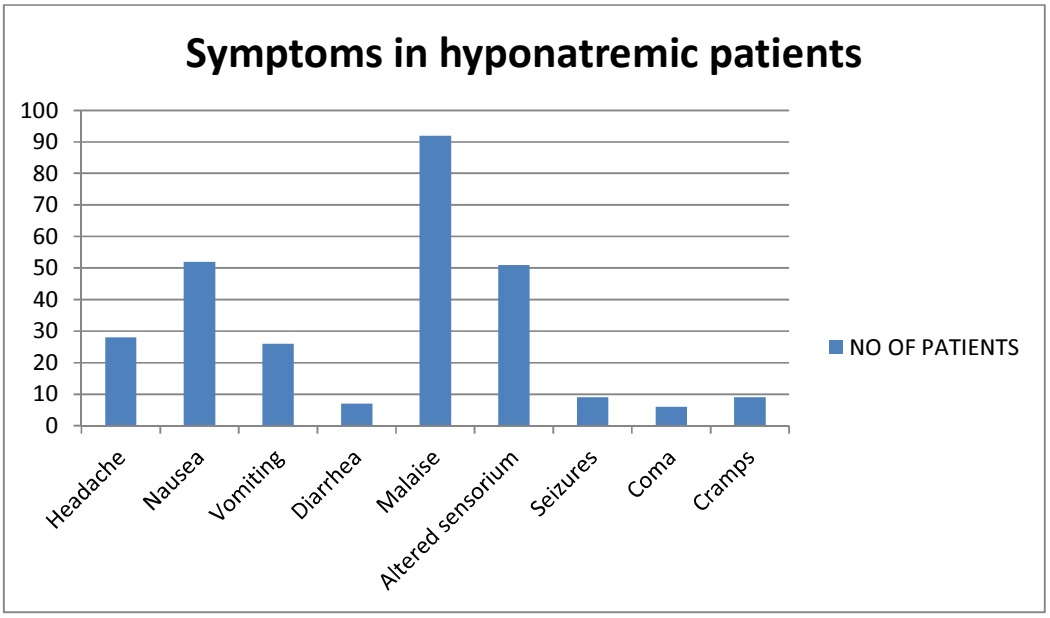

Figure 7

TABLE 8: SYMPTOMS IN MALES

SYMPTOMS	NO OF PATIENTS
Malaise	55
Nausea	33
Altered sensorium	33
Headache	18
Vomiting	17
Seizures	4
Coma	4
Cramps	3
Diarrhea	2

Out of 57 patients, 18 had headache, 33 had nausea, 17 had vomiting, 2 had diarrhea, 55 had malaise, 33 had altered sensorium, 4 had seizures, 4 had coma and 3 had cramps.

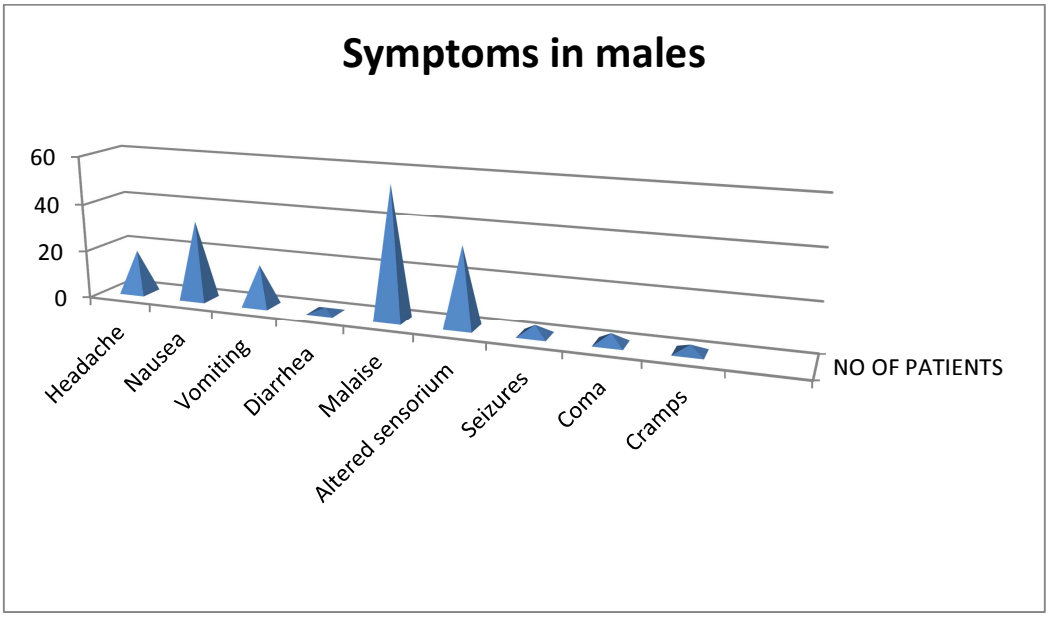

Figure 8

TABLE 9: SYMPTOMS IN FEMALES

SYMPTOMS	NO OF PATIENTS
Headache	10
Nausea	19
Vomiting	9
Diarrhea	5
Malaise	37
Altered sensorium	18
Seizures	5
Coma	2
Cramps	6

Out of 43 female patients, 10 had headache, 19 had nausea, 9 had vomiting, 5 had diarrhea, 37 had malaise, 18 had altered sensorium,5 had seizures , 2 had coma and 6 had cramps

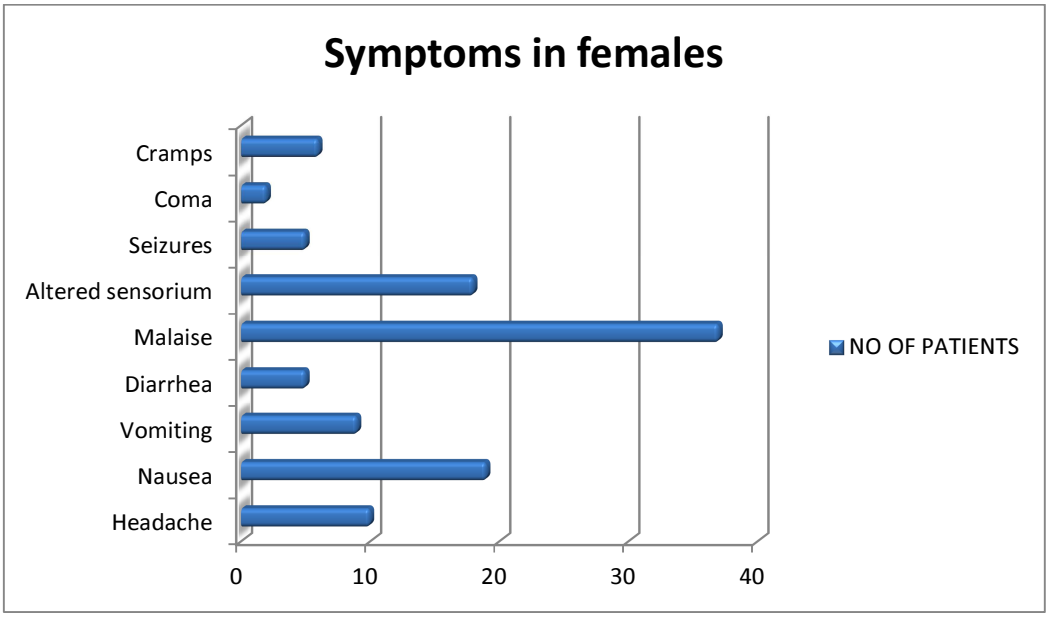

Figure 9

TABLE 10: SEVERITY OF HYPONATREMIA

SERUM SODIUM(in mEq/l)	NO OF PATIENTS
105-115	7
116-125	33
126-134	60

SEVERITY OF HYPONATREMIA:

Out of 100 patients, 60 had serum sodium levels between 126-134 mEq/litre, 33 had serum sodium levels between 116-125 mEq/litre, 7 had serum sodium levels in between 105-115 mEq/litre.

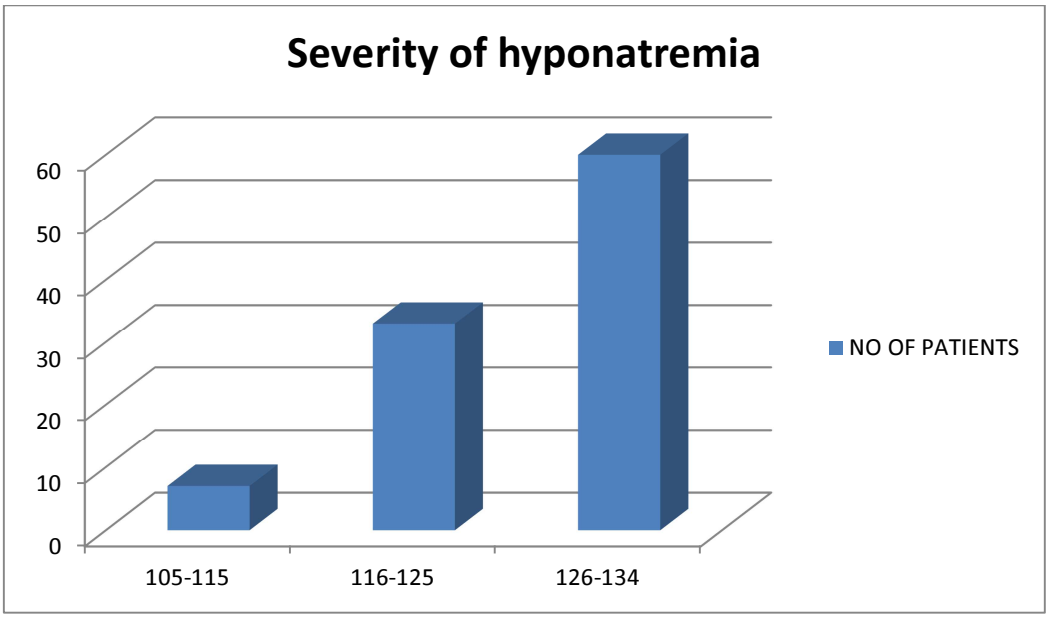

Figure 10

TABLE 11: SEVERITY IN MALES

SERUM SODIUM(in mEq/l)	NO OF PATIENTS
105-115	3
116-125	22
126-134	32

SEVERITY IN MALES:

Out of 57 male patients,32 patients had serum sodium level between 126-134 mEq/litre, 22 patients had serum sodium levels between 116-125 mEq/litre and 3 patients fall in between serum sodium levels of 105 -115 mEq/litre.

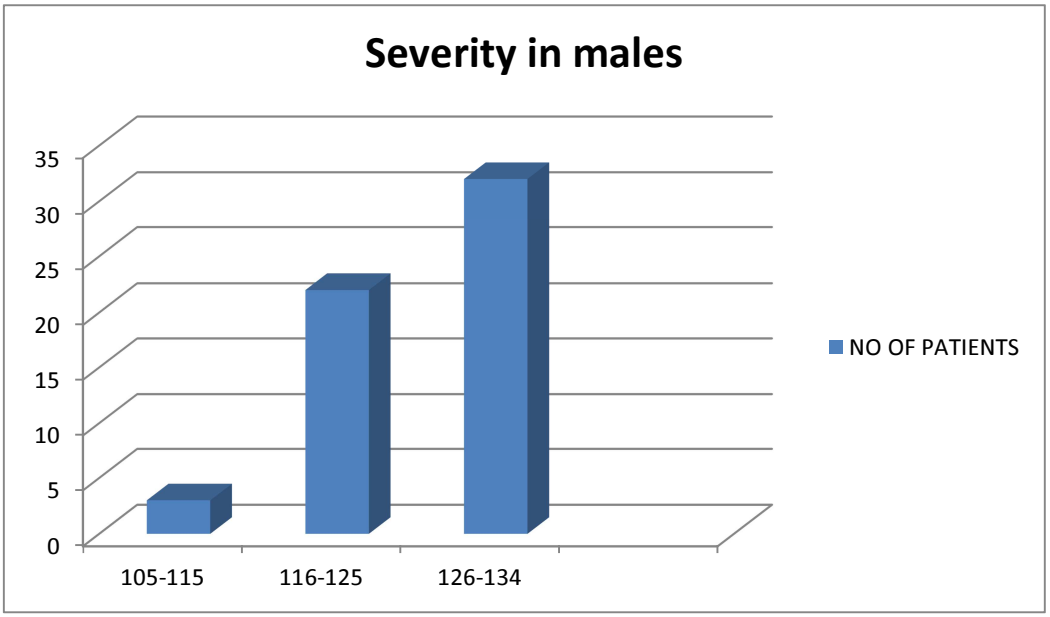

Figure 11

TABLE 12: SEVERITY IN FEMALES

SERUM SODIUM(In mEq/l)	NO OF PATIENTS
105-115	4
116-125	11
126-134	28

SEVERITY IN FEMALES:

Out of 43 female patients, 28 patients had serum sodium levels between 126-134 mEq/litre, 11 patients had serum sodium levels between 116-125 mEq/litre and 4 patients fall between serum sodium levels of 105-115 mEq/litre.

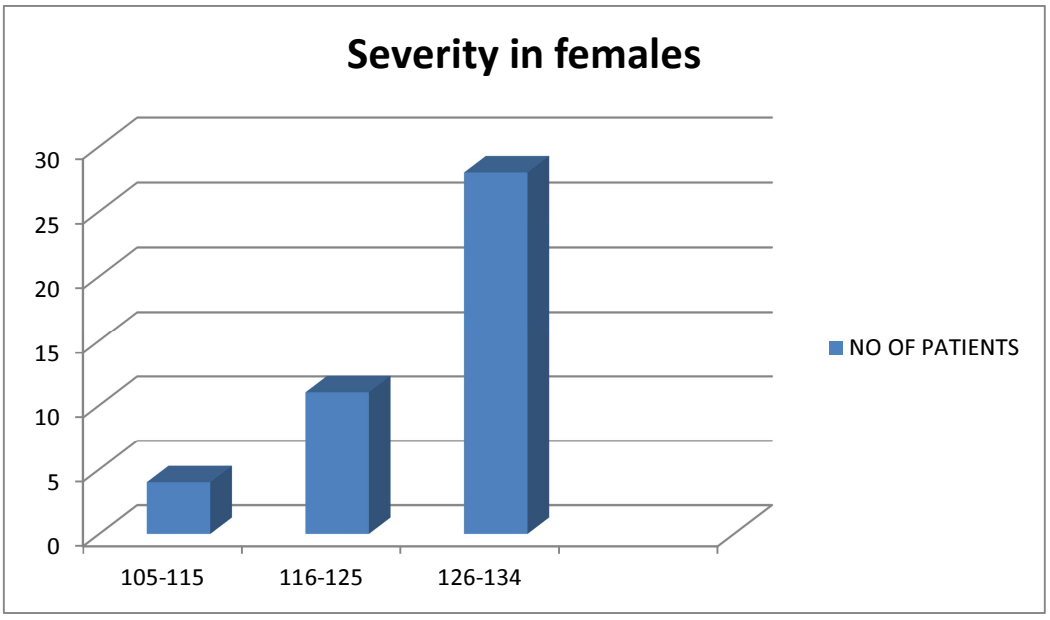

Figure 12

TABLE 13: HYDRATION STATUS

HYDRATION STATUS	NO OF PATIENTS
EUVOLEMIC	42
VOLUME OVER LOAD	31
HYPOVOLEMIA	27

HYDRATION STATUS:

Out of 100 patients, 42 patients showed normal hydration status, 31 patients were in volume overload status and 27 patients were dehydrated. (table 13 and figure 13).

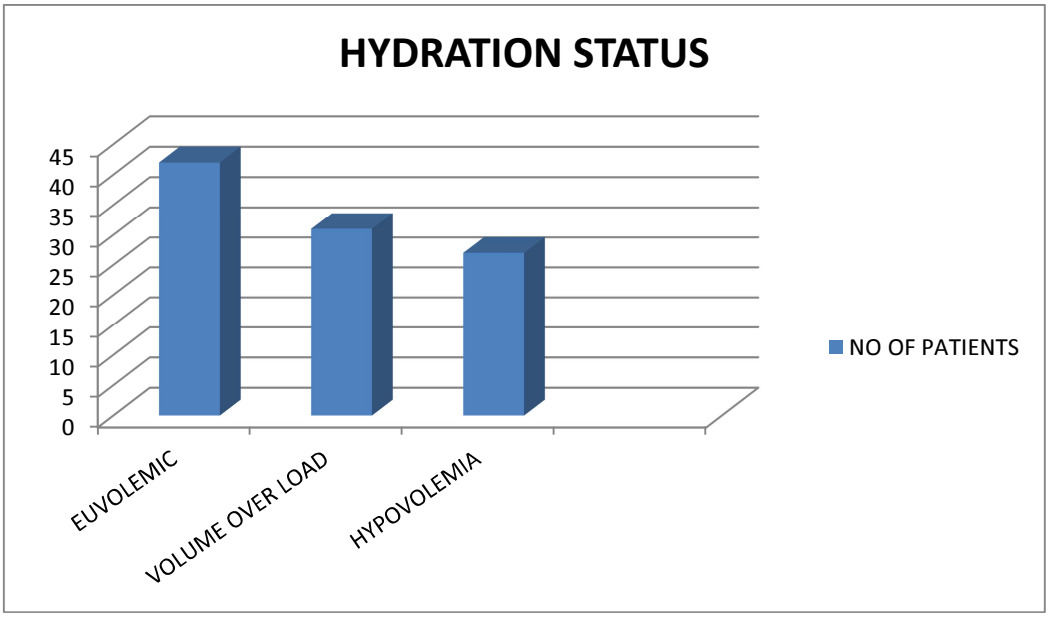

FIG 13: HYDRATION STATUS

TABLE 14: TYPES OF HYPONATREMIA

TYPES OF HYPONATREMIA	NO OF PATIENTS
HYPOOSMOLAR- EUVOLEMIC	42
HYPOOSMOLAR- HYPERVOLEMIC	31
HYPOOSMOLAR- HYPOVOLEMIC	27

TYPES OF HYPONATREMIA

Out of 100 patients, 42 patients had hypoosmolar euvolemic hyponatremia, 31 patients had hypoosmolar hypervolemic hyponatremia and 27 patients had hypoosmolar hypovolemic hyponatremia.

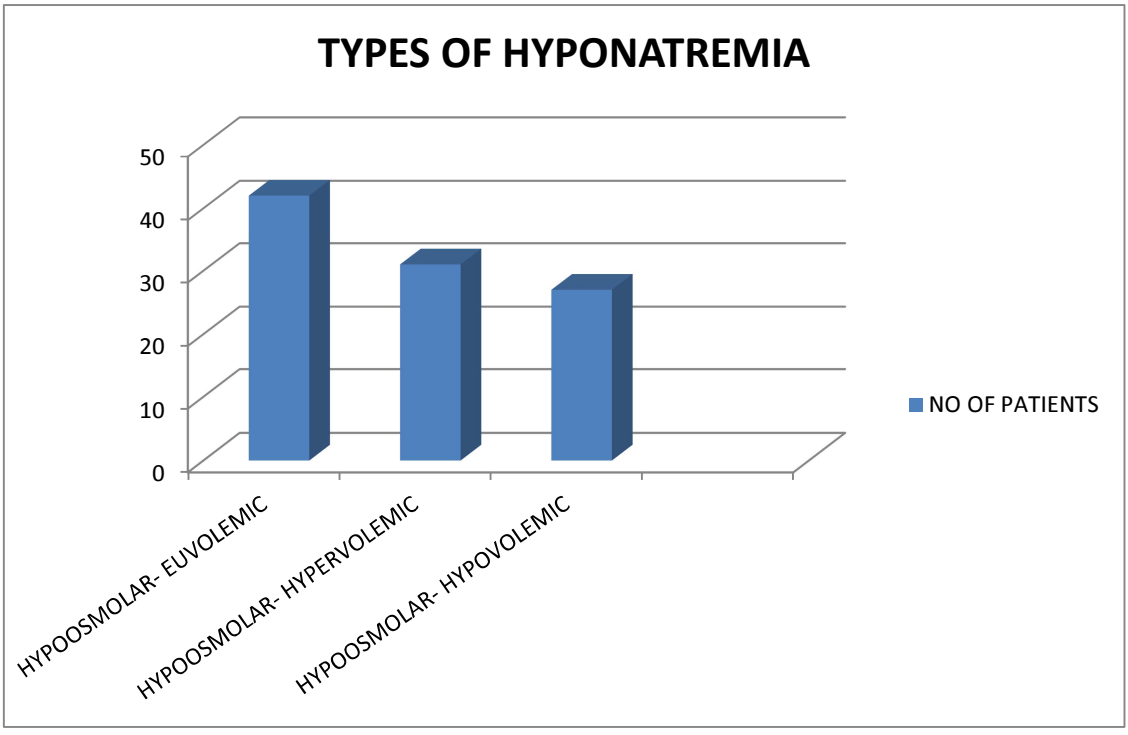

FIG 14: TYPES OF HYPONATREMIA

TABLE 15: TYPES OF HYPONATREMIA IN MALES

TYPES OF HYPONATREMIA	NO OF PATIENTS
HYPOOSMOLAR- EUVOLEMIC	25
HYPOOSMOLAR- HYPERVOLEMIC	18
HYPOOSMOLAR- HYPOVOLEMIC	14

TYPES OF HYPONATREMIA IN MALES:

Out of 57 patients, 25 patients had hypoosmolar euvolemic hyponatremia, 18 patients had hypoosmolar hypervolemic hyponatremia and 14 patients had hypoosmolar hypovolemic hyponatremia.

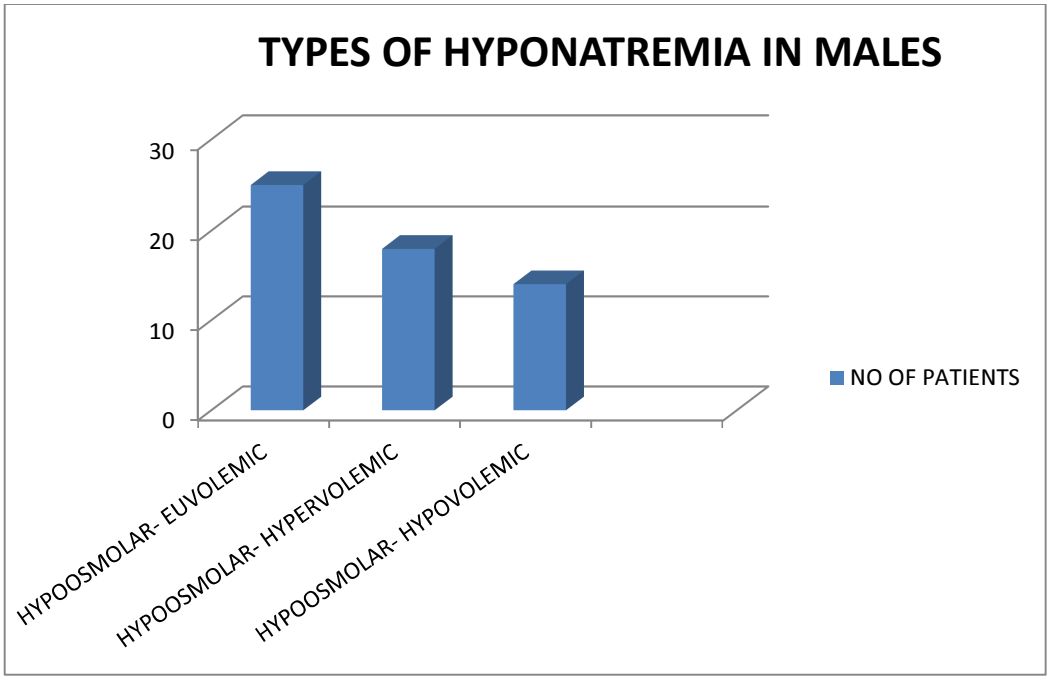

FIG 15: TYPES OF HYPONATREMIA IN MALES

TABLE 16: TYPES OF HYPONATREMIA IN FEMALES

TYPES OF HYPONATREMIA	NO OF PATIENTS
HYPOOSMOLAR- EUVOLEMIC	17
HYPOOSMOLAR- HYPERVOLEMIC	13
HYPOOSMOLAR- HYPOVOLEMIC	13

TYPES OF HYPONATREMIA IN FEMALES:

Out of 43 patients, 17 patients had hypoosmolar euvolemic hyponatremia, 13 patients had hypoosmolar hypervolemic hyponatremia and 13 patients had hypoosmolar hypovolemic hyponatremia. (Table 16 and figure 16).

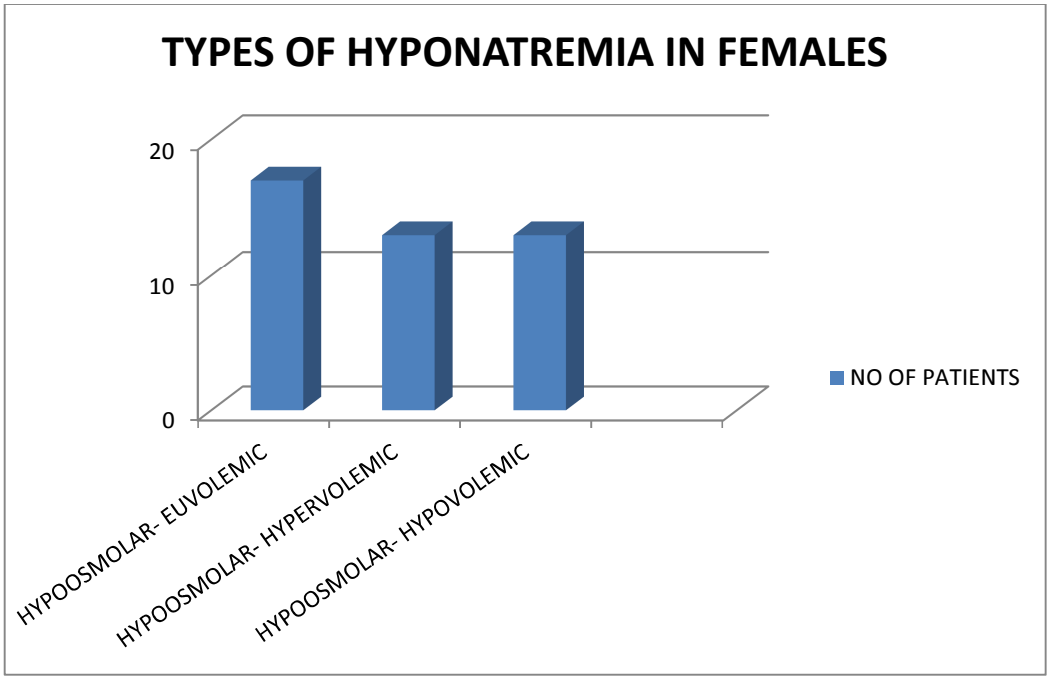

FIG 16: TYPES OF HYPONATREMIA IN FEMALES

TABLE 17: ETIOLOGY OF EUVOLEMIC HYPONATREMIA

CAUSES	NO. OF PATIENTS	
	MALES	FEMALES
SIADH	23	12
ADRENAL INSUFFICIENCY	1	0
HYPOTHYROIDISM	0	4
FLUOXETINE	0	1
CARBAMAZEPINE	1	

ETIOLOGY OF EUVOLEMIC HYPONATREMIA:

Out of 42 patients with euvolemic hyponatremia, 35 patients had SIADH (23 were males and 12 were females), 4 patients had hypothyroidism (females), 1 patient had adrenal insufficiency (male) and drugs causing inappropriate ADH secretion in 2 patients (1 male and 1 female)

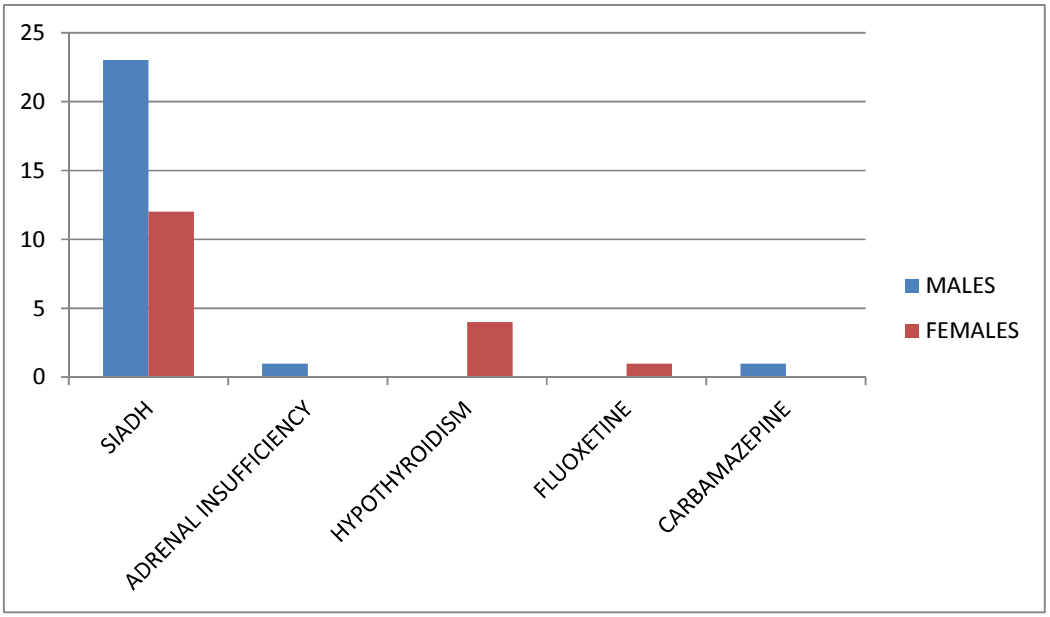

FIG 17: ETIOLOGY OF EUVOLEMIC HYPONATREMIA

TABLE 18: ETIOLOGY OFHYPERVOLEMIC HYPONATREMIA

CAUSES	NO. OF PATIENTS	
	MALES	FEMALES
RENAL	12	9
CARDIAC FAILURE	3	4
CIRRHOSIS	2	0
NEPHROTIC SYNDROME	1	0

ETIOLOGY OF HYPERVOLEMIC HYPONATREMIA:

Out of 31 patients, 21 were due to renal causes (12 were males and 9 were females), 7 were due to cardiac failure (3 were males and 4 were females), 2 were due to cirrhosis (male) and1 was due to nephritic syndrome (male).

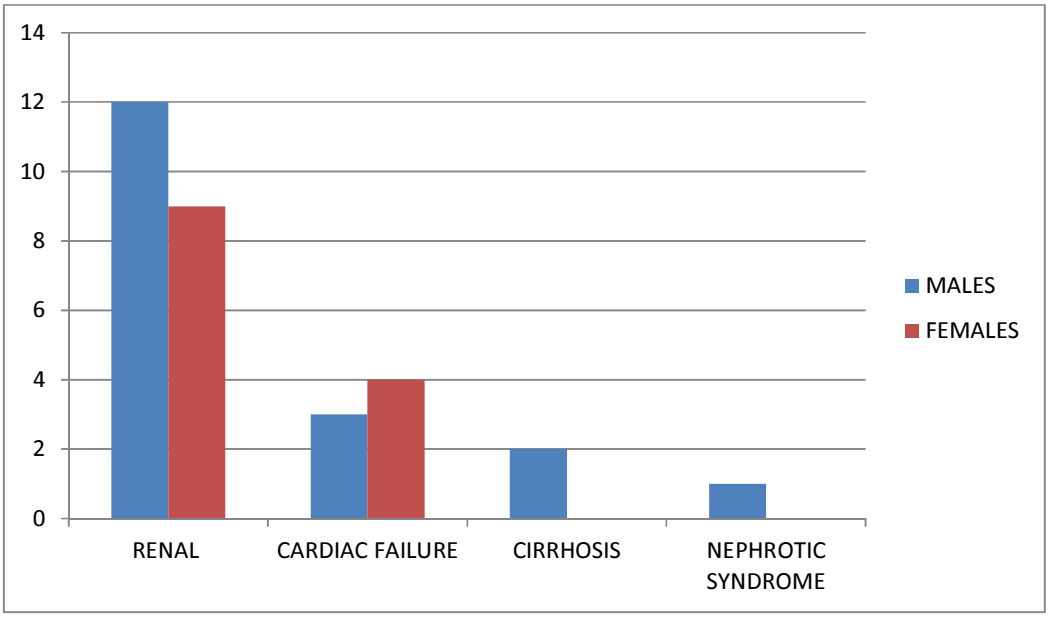

FIG 18: ETIOLOGY OF HYPERVOLEMIC HYPONATREMIA

TABLE 19: ETIOLOGY OF HYPOVOLEMIC HYPONATREMIA

CAUSES	NO. OF PATIENTS	
	MALES	FEMALES
GI LOSS	8	9
DIURETIC EXCESS	4	4
PANCREATITIS	1	0
RTA	1	0

ETIOLOGY OF HYPOVOLEMIC HYPONATREMIA:

Out of 27 patients, 17 were due to GI loss (8 males and 9 females), 8 were due to diuretic excess (4 males and 4 females), 1 was due to pancreatitis (male) and 1 was due to renal tubular acidosis (male).

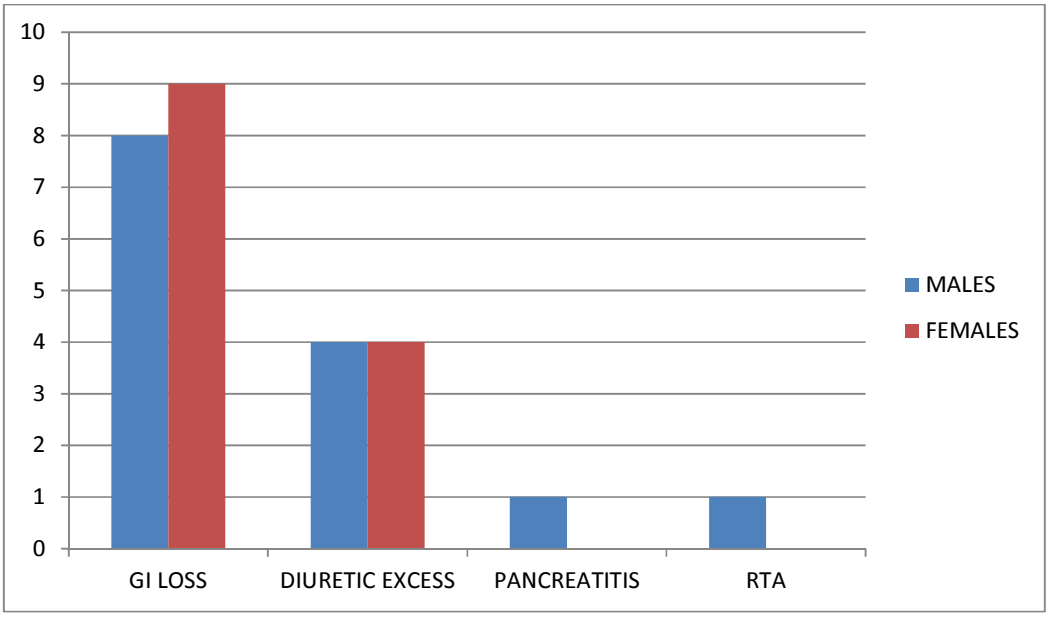

FIG 19: ETIOLOGY OF HYPOVOLEMIC HYPONATREMIA

TABLE 20: MEAN AGE OF HYPONATREMIC PATIENTS

SEX	MEAN AGE
MALES	72.40±7.01
FEMALES	72.23±6.02
TOTAL	72.33±6.57

MEAN AGE OF PATIENTS:

The mean age of hyponatremic patients in this study is 72.33±6.57.

The mean age of hyponatremic males is 72.40±7.01.

The mean age of hyponatremic females is 72.23±6.02.

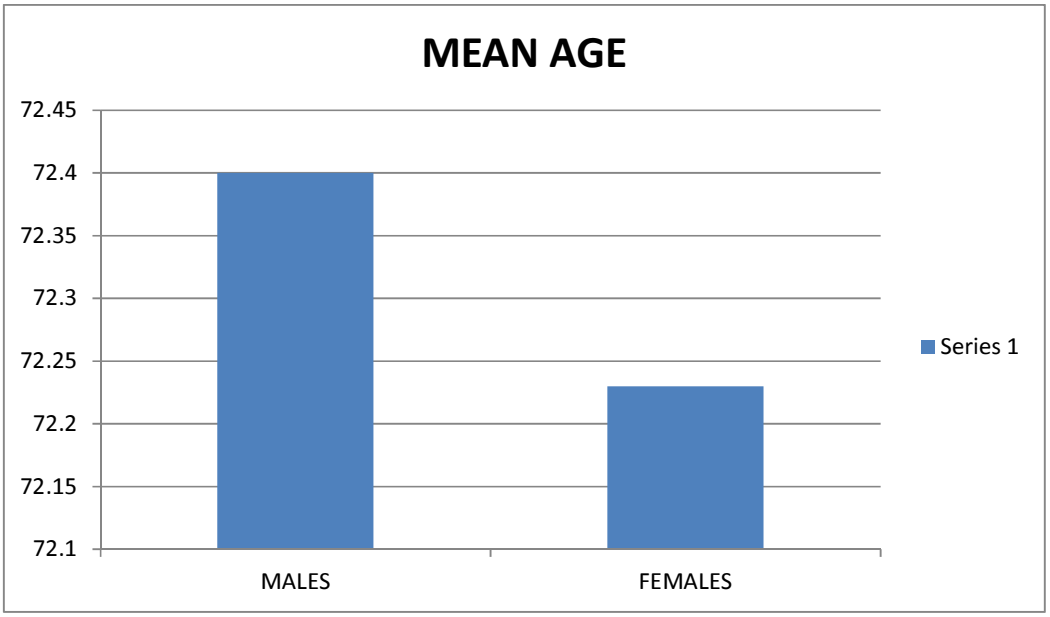

FIG 20: MEAN AGE OF HYPONATREMIC PATIENTS

TABLE 21: MEAN SERUM SODIUM IN HYPONATREMIC PATIENTS

SEX	MEAN SERUM SODIUM
MALES	125.01±6.56
FEMALES	126.21±7.10
TOTAL	125.55±6.79

MEAN SERUM SODIUM IN HYPONATREMIC PATIENTS:

The mean serum sodium level in hyponatremic patients in this study is 125.55±6.79 mEq/litre

The mean serum sodium level in males is125.01±6.56

The mean serum sodium level in females is 126.21±7.10.

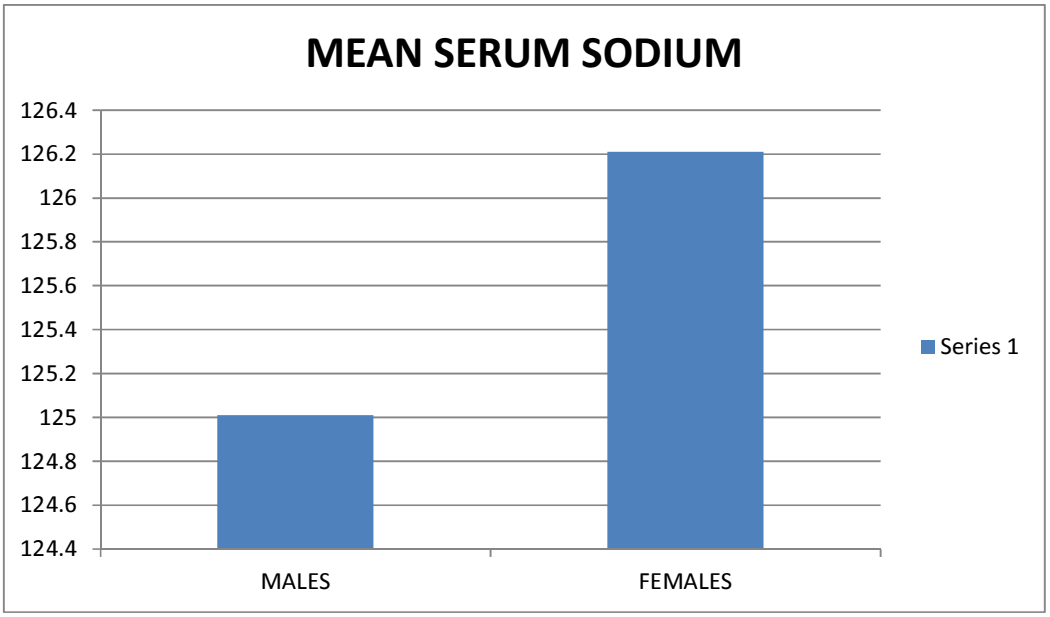

FIG 21: MEAN SERUM SODIUM IN HYPONATREMIC PATIENTS

TABLE 22: MEAN SERUM OSMOLALITY IN HYPONATREMIC PATIENTS:

SEX	MEAN SERUM OSMALITY
MALES	261.88±11.76
FEMALES	263.63±12.23
TOTAL	262.63±11.9

MEAN SERUM OSMOLALITY IN HYPONATREMIC PATIENTS;

The mean serum osmolality in hyponatremic patients in this study is 262.63±11.9.

The mean serum osmolality in males is 261.88±11.76

The mean serum osmolality in females is 263.63±12.23

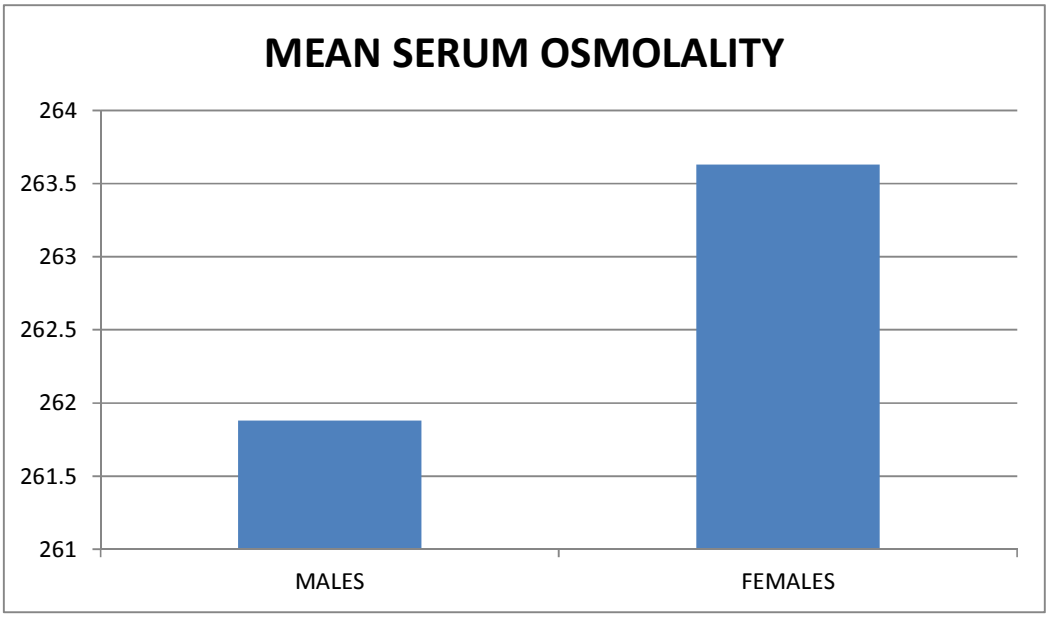

FIG 22: MEAN SERUM OSMOLALITY IN HYPONATREMIC PATIENTS

TABLE 23: MEAN DURATION OF ILLNESS AT PRESENTATION

SEX	MEAN DURATION OF ILLNESS
MALES	6.1±5.09
FEMALES	7.95±8.26
TOTAL	6.9±6.67

Mean duration of illness at presentation is 6.9±6.67

Mean duration of illness in males is 6.1±5.09

Mean duration of illness in females is 7.95±8.26

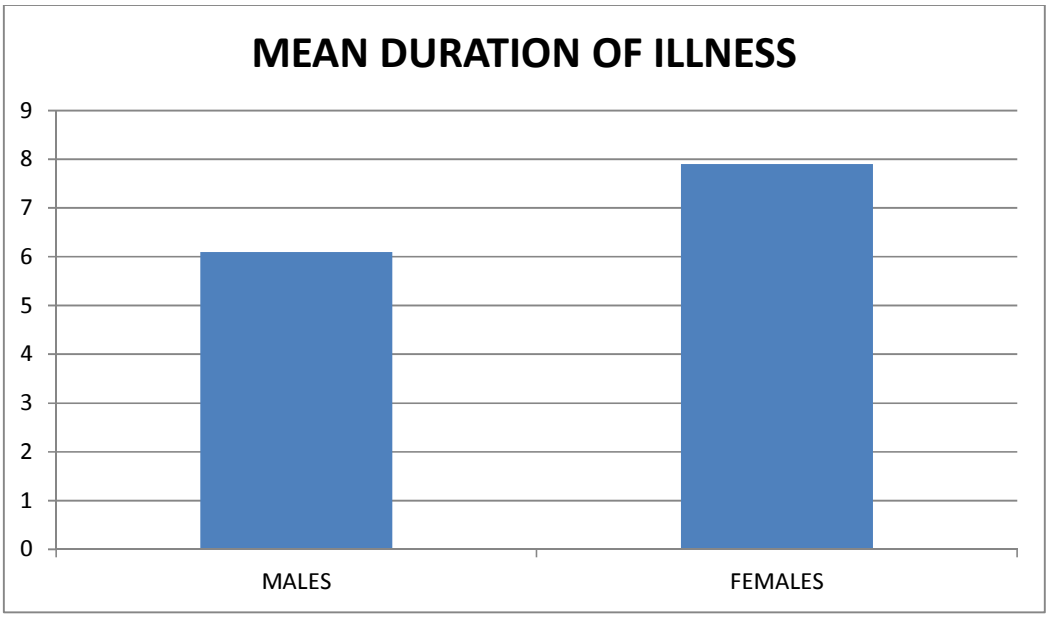

FIG23: MEAN DURATION OF ILLNESS AT PRESENTATION

DISCUSSION

This study was conducted in a tertiary care hospital. 100 cases admitted in the hospital having serum sodium less than 135 mEq/litre were included in the study.

The mean age of this study population is 72 with a standard deviation of 6. This mean age is similar to mean age of studies conducted by Richard h sterns et al, sudir m y rao et al etc.

Regarding the different types of hyponatremia, In a study of 66 elderly patients conducted by Anderson et al, in geriatric age group, 34% had euvolemic hyponatremia, 19 % had hypervolemic hyponatremia, 17 % had hypovolemic hyponatremia. Various studies conducted throughout the world say that euvolemic hyponatremia is the commonest cause of hyponatremia in elderly subjects. In a study conducted by Sengupta , nandhini chatterjee et al in eastern part of India in 201 hyponatremic patients, 50.74% patients had euvolemic hyponatremia followed by 26.86% of patients having hypervolemic hyponatremai and 22.4% patients having hypovolemic hyponatremia. In this study also euvolemic hyponatremia appears to be the commonest cause with 42 percentages of patients being euvolemic, followed by hypervolemic hyponatremia of 34 percent and next by hypovolemic hyponatremia of 27 percentage.

Laczi et al in their study in Hungary suggested that SIADH is the most common cause of hyponatremia in euvolemic subjects. A study conducted by CJ Thompson et al, in Dublin Ireland also suggests that SIADH is the commonest cause of hyponatremia in hospitalized patients. In this study also SIADH appears to be the most common cause of euvolemic hyponatemia with 35 patients out of 42 euvolemic patients having this syndrome.

In this study the commonest cause of hypervolemic hyponatremia is renal cause with 21 out of 31 patients with hypervolemic hyponatremia. The other causes include congestive cardiac failure and cirrhosis. This is similar to the study outcomes in the study conducted by M Y rao et al in India. Several studies show diuretics especially thiazide, when used in excess and inappropriately in geriatric age group cause hyponatremia. This view is supported by the study conducted in Rochester university USA out of 200 patients with thiazide diuretic 83 patients found to have hyponatremia due to erroneous usage of thiazide diuretics. In this study 8 patients were found to have hyponatremia due to excess use of diuretics. Out of 8 patients four were male and four were female. In seven patients hyponatremia is due to thiazide diuretic and in one patient hyponatremia is due to loop diuretic.

In this study GI loss accounts for the major cause of fluid loss in hypovolemic hyponatremia. The commonest route of fluid loss is through vomiting with 26 patients having vomiting and in 7 patients fluid is lost due to diarrhoea. Out of 40 patients with serum sodium levels below 125 mEq/litre, 15 patients had severe CNS symptoms like seizure and coma. The other central nervous system symptoms are lethargy, headache, altered level of consciousness. The other symptoms are nausea , vomiting, diarrhoea and muscle cramps. Of these the commonest symptom is nausea with 52 patients having nausea. In this study the common comorbid illnesses are hypertension, diabetes mellitus, chronic kidney disease and coronary artery disease. Of this hypertension is present in 52 patients (32 are male and 20 are females), diabetes mellitus is present in 28 patients (15 are males and 13 are females), coronary artery disease is present in 18 patients (12 are males and 6 are females), Chronic kidney disease is present in 11 patients (6 are females and 5 are males). This comorbid illness is similar to the comorbid illness result found in study conducted by sarvanan, sudhi et al in India. In their study, 62 percent of comorbid illness is hypertension and 51 percent were diabetes mellitus and 22 percent were renal failure patients and 18 percent were coronary artery disease patients.

LIMITATIONS OF THE STUDY

- Duration of study is 6 months
- Study population is only100 patients
- It is a hospital based observational study so there is difficulty in identifying asymptomatic hyponatremia in community dwelling elderly
- The volume status of the patient is assessed clinically which is not a precise method of estimation.

CONCLUSION

Incidence of hyponatremia is high among elderly when compared to young adults. This is attributed to the fact that, when elderly persons are exposed to a change in environment and an altered dietary practice, there is impairment in their ability to maintain an optimal balance of water and electrolytes. The etiology of hyponatremia among geriatric age group is complex and it is further complicated by an unclear relationship between arginine vasopressin and advancing age

Factors contributing to the development of hyponatremia in the elderly patients include an age associated decrease in free water excretion and GFR. There is sodium loss with aging. This is contributed by decreased action of RAAS and exaggerated action of natriuretic hormones.

Development of severe hyponatremia is associated with high morbidity and high mortality. This is especially high with elderly patients.

Hence early identification and assessment of different types of hyponatremia in elderly patient is very important to improve the patient outcome.

BIBLIOGRAPHY

1. Verbalis JG, Berl T: Disorders of water balance. In: *Brenner & Rector's The Kidney,* 8th Ed., edited by Brenner BM, Philadelphia, Saunders Elsevier, 2008, pp 459–504

2.Janicic N, Verbalis JG. Evaluation and management of hypoosmolality in hospitalized patients. *Endocrinol Metab Clin North Am* 2003;32:4

3.Crawford GA, Johnson AG, Gyory AZ, Kelly D. Change in arginine vasopressin concentration with age. *Clin Chem* 1993;39:2023.

4. Arinzon Z,Feldman J,Bener Y : Peisat A,Zuta A ; Water and sodium disturbances predict prognosis of acute disease in long term care frail elderly, Arch Geront,Geriatrics 40 : 317-326;2005

5.SandyCraig,2003"hyponatremia",Emedicine specialities,http:/www.emedicine.com/emerg/topic275.htm.section 1-10.

6. John P Kugler,et al, 2000. "Hyponatremia and hyponatremia in the elderly" American Family Physics;61:362 3-30

7. Gill G,Huda B,Boyd A,SkagenK,Wile D,Watson I & Von Heyningen C, Characteristics and Mortality of Severe Hyponatremia- a hospital based study.Clinical Endocrinology 2006[65] 246-249

8.Miller M,Morley JE,Rulkenstein L2,hyponatremia in a nursing home population, J Am Geriatric Society . 1995;43:1410-1413

9.Mann,J.F.E et al (1987) Triss st & RAAS, Kidney Internatinal Supplement 21.,

10.Robertson G.L (1987) Physiology of ADH Secretion,Kidney international supplement 21

11.Leng G., Mason Wt, Dyer RG The Supraoptic Nucleus As An Osmoreceptor Neuroendocrinology 1982;34:75-82

12.Buggy J,Johnson AK: Preoptic Hypothalamic Periventricular Lesions Thirst Deficit & Hypernatremia (AMJ Physio 233,R 44-R 52)

13.Thrasher et al : Lesion of OVLT attenuation osmotically induced drinking and vasopressin secretion in the dog.Endocrinology 1982,110:1837-1839

14.Baylis,P.H.(1987) Osmoregulation And Control Of Vasopressin Secretion In The Healthy Humans American Journal Of Physiology 253 (R 671)

15.Anderson Mc Et al : Cellular Mechanism Of Baroreceptor Integration at the NTS Ann Ny Academy Science 2001;940:132-141

16.Renaul LP: CNS Pathway Mediating Cardiovascular Regulation of Vasopressin Clin Exp.Pharmacology Physiology 1996;23:157-160

17.Abramow M,et (1987) cellular events in vasopressin action kidney international supplement 21,

18.Salata RA,Robinson AG, Cold water stimulation of oropharyngeal receptors in man inhibiting release of vasopressin

19.Rowe,Shelton et al : Influence of Emetic Reflex on Vasopressin Release in Man,Kidney Internation 1979;729-735

20.Baylis PH,AVP response to insulin induced hypoglycaemia in man J Clin Endocrino Metabolism 1981;53:935-940

21.Keil LL,Sever WB:Release of vasopressin by angiotensin II (Endocrinology 1975) 96:1063-1065

22.Mckinley MJ, McAllen RM,Pennington Gl,et al : Physiological action of angiotensin II mediating by AT I & AT 2 receptors in the brain, Clin Exp Pharmacology Physiology Supplement 1996;3-S 99- S 104

23.Mckiney et al Brain angiotensin & body fluid homeostasis JPN J physiology 2001;51:281-289

24.Baylis Ph ,Health DA:effect of acute hypoxemia on plasma AVP in conscious man,Clin Sci Mol Med 1977;53:401-404

25.Clay Bayn DR,Hasen JE,Wornial DB:Response of antidiuretic hormone to acute exposure to mild & severe hypoxia in man : J Endocrinology 1978;TT 157-160

26.Farber MO,Weinberger MH,Robessa GE et al: hormonal abnormalities affecting sodium and water balance in acute respiratory failure due to chronic lung disesase chet 1904;85:49-54

27.Agree 2000:Aquaporin water channels in kidney Journal Of Society Of Nephrology 11

28.Deen et al 1994:Requirement of renal water channel aquaporin 2 for vasopressin dependant concentration of urine

29.Harris et al 1991:Current understudy of cellular biopsy of ADH stimulated water transport pathway J of clinical investigation 88

30.Bonvalet et al 1987 Yered et al 1985: Segmental synthesis & action of PG along the nephron Am J of physiology

31.Herbert et al 1990 :PGE_2 AVP induced water flow in cortical collecting duct by protein kinase C activation Am J of physiology 259

32.Miller M,Gold :Physiological changes of aging affecting salt and water balance Rev Clinical Gerontology 1991;1:215

33.Asplund R,Aberg H, diurnal variations in levels of antidiuretic hormone in the elderly J Intermed 1991;299:131

34.Johnson AG,Arginine vasopressin and osmolality in the elderly J Am Geriatric soc 1994;42:399

35.Helderman JH,Vestal RE.Rowejw,et al:the response of AVP to intravenous ethanol and hypertonic saline in man.The impact of aging.J Gerontol,1978;33:39

36.J.M Sands & Koko J.P.(1996).Current concept of the countercurrent multiplication system,Kidney Internation supplement 57; S93-S99

37.Zimmerhackel.B. Robertson C.R & Jamison R.L (1985).Fluid uptake in the renal papilla by vasa recta estimated by two methods;Am J of physiology 248; F 347- F 353

38.Espiner EA,Richard Am,Yandle TG et al,Natriuretic hormones,Endocrinal metabolism clinics North Am 1995;24:481

39.Bauer JH;Age related change in RAAS,Physiological effect & clinical implication drugs aging 1993;3:238

40.Sterns R: Sodium & water balance disorder nephrology SAP 2006;5:35-50

41.Chow KM,Kwan BC,Szeto CC:Clinical studies of thiazide induced hyponatremia J national Med Association 2004:96:1305-1308

42.Rosin AJ:dieuretic induced severe hyponatremia-Review and analysis of 129 reported patients;1993;103:601

43.Clark B,Shannon R,Rosa r,Increased susceptibility of thiazide induced hyponatremia in the elderly,J Am Soc Nephrology 1994;5:1106

44.Danovihcb GM,Bougoignie J,Briclav NS; Reversibility of salt loosing tendency of CRF NETN 1977;296:4

45.Atkin SL et al 1996:Hyponatremia secondary to cerebral salt wasting syndrome following routine pituitary sugar.European Journal of Endocrinology 135 940-946

46.Schrierw RW 1988:Pathogenesis of sodium & water retention in high output and low output cardiac failure;nephrotic syndrome,cirrhosis & pregnancy

47.Leier CV,Dei cas.L,Metra M 1994:Clinical relevance and management of the major electrolyte abnormalities in congestive heart failure.hyponatremia,hypokalemia and hypomagnesemia.American Heart Journal 128:564-574

48.Dzau & Hollenberg 1984:Renal response to captopril in severe heart failure;Role of furosemide in natriuresis and reversal of hyponatremia.Annals of Internal medicine 100:777-782

49.Gives P,Berl T,Bernadi M et al:Hyponatremia in cirrhosis from pathogenesis to treatment hepatology 1988;28:851-864

50.T Suboi Y et al 1994:Therapeutic efficacy of the nan peptide AVP antagonist in cirrhotic rats Kidney International 46,237-294

51.Papadakis MA,Fraser CL,Arieff AI 1990 hyponatremia in patients with cirrhosis;Q century journal of medicine 76; 675-688

52.Abraham,Schrier RW,Cardiac failure,liver diseases and nephrotic syndrome,Diseases of kidney 7th edition 2001:2465

53.Zimmerman et al 1987:Anatomic basis of thirst & vasopressin secretion Kidney International Supplement 21: S 14- S 19

PREVALENCE AND EVALUATION OF HYPONATREMIA

IN ELDERLY PATIENTS

Name: Age: Sex:

Address: Occupation:

Duration and details of illness:

Symptoms:

- Headache
- Nausea
- Vomiting
- Diarrhea
- Muscle weakness
- Muscle cramps
- Malaise
- Altered level of consciousness

- Seizures
- Coma

PAST HISTORY:

- Hypertension
- Diabetes
- CAD
- Tuberculosis
- Hypothyroidism
- Hyperlipidemia
- Ckd

DRUG HISTORY:

PERSONAL HISTORY:

☐ Smoking ☐ Alcoholism

CLINICAL SETTING:

GENERAL EXAMINATION:

VITALS

VOLUME STATUS

- PULSE
- BLOOD PRESSURE
- MUCUS MEMBRANES - DRY/MOIST
- URINE OUTPUT
- JVP
- HEPATOJUGULAR REFLEX
- COLD AND CLAMMY EXTREMITIES - YES/ NO
- PERIPHERAL EDEMA
- Ascites
- PULMONARY CONGESTION
- CAPILLARY REFILL

SYSTEMIC EXAMINATION:

CVS:

RS:

ABDOMEN:

CNS:

INVESTIGATIONS:

Hb: TC: DC: P- L- E- M- Plt:

ESR:

Blood Glucose Random :

Blood Urea :

Serum Creatinine :

Serum Electrolytes : Na+ K+

Serum osmalalitY :

URINE EXAMINATION:

Sugar :

Deposits :

Albumin :

Sodium :

ECG:

X-RAY CHEST PA VIEW :

<u>ஆராய்ச்சி தகவல் தாள்</u>

சென்னை இராஜிவ் காந்தி அரசு பொது மருத்துவமனைக்கு வரும் 65 வயதுக்கு மேற்பட்ட முதிய நோயாளிகளுக்கு ஏற்படும் சோடியம் குறைபாடு பற்றிய ஒரு ஆராய்ச்சி நடைபெற்று வருகிறது.

முதிய நோயாளிகளுக்கு இந்த சோடியம் குறைபாடு என்பது எவ்வளவு பரவலாக இருக்கிறது என்பது பற்றியும், அதற்கான காரணங்கள் என்ன என்பது பற்றியும் அறிந்து கொள்வதே இந்த ஆராய்ச்சியின் நோக்கமாகும்.

நீங்களும் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம். முடிவுகளை அல்லது கருத்துக்களை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருத்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த சிறப்புப் பரிசோதனைகளின் முடிவுகளை ஆராய்ச்சியின் போது அல்லது ஆராய்ச்சியின் முடிவில் தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

தேதி:

<u>ஆராய்ச்சி ஒப்புதல் கடிதம்</u>

ஆராய்ச்சி தலைப்பு:

65 வயதுக்கு மேற்பட்ட முதிய நோயாளிகளுக்கு ஏற்படும் சோடியம் குறைபாடு பற்றிய ஆராய்ச்சி.

பெயர்: தேதி:

வயது: உள்நோயாளி எண்:

பால்: ஆராய்ச்சி சேர்க்கை எண்:

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது. எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்து கொண்டு நான் எனது சம்மதத்தை தெரிவிக்கிறேன்.

சோடியம் குறைபாட்டின் அறிகுறிகள் மற்றும் பாதிப்புகள் குறித்து ஆராய்ச்சியாளர் கூற முழுவதும் விளங்கப்பெற்றேன்.

இதற்குத் தேவையான உடற்பரிசோதனைக்கும், இரத்தம் சம்பந்தப்பட்ட பரிசோதனைகளுக்கும் மனமார சம்மதிக்கிறேன்.

கையொப்பம்

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. Karthieyan .A
PG in MD Geriatrics
Madras Medical College, Chennai -3

Dear Dr. Karthieyan .A

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "Prevalence and evaluation of hyponatremia in elderly patients " No.29062012.

The following members of Ethics Committee were present in the meeting held on 19.06.2012 conducted at Madras Medical College, Chennai -3.

1.	Dr. S.K. Rajan. M.D.,FRCP.,DSc	-- Chairperson
2.	Prof. K. Ramadevi MD Prof of Biochemistry, MMC, Ch-3	-- Member
3.	Prof. R. Nandhini MD Director, Inst. of Pharmacology ,MMC, Ch-3	-- Member
4.	Prof. C. Rajendiran, MD Director , Inst. of Internal Medicine, MMC, Ch-3	-- Member
5.	Prof. S. Deivanayagam MS Prof of Surgery, MMC, Ch-3	-- Member
6.	Prof. A. Radhakrishnan MD Prof of Internal Medicine, MMC, Ch-3	-- Member

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

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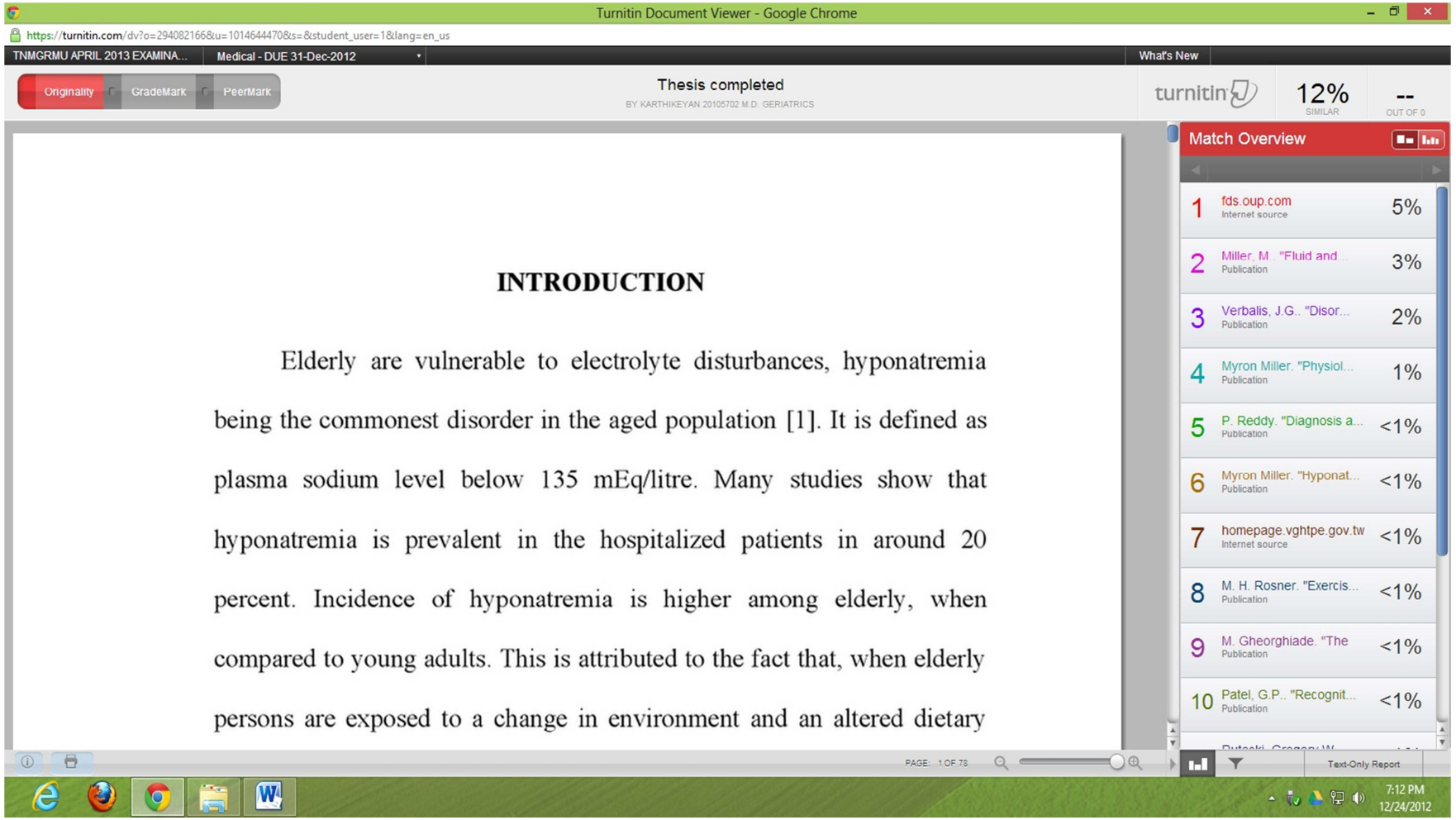
INTRODUCTION Elderly are vulnerable to electrolyte disturbances, hyponatremia being the commonest disorder in the aged population [1]. It is defined as plasma sodium level below 135 mEq/litre. Many studies show that hyponatremia is prevalent in the hospitalized patients in around 20 percent. Incidence of hyponatremia is higher among elderly, when compared to young adults. This is attributed to the fact that, when elderly persons are exposed to a change in environment and an altered dietary practice, there is impairment in their ability to maintain an optimal balance of water and electrolytes [2]. Factors contributing to the development of hyponatremia in the elderly patients include an age...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INTRODUCTION
Elderly are vulnerable to electrolyte disturbances, hyponatremia being the commonest disorder in the aged population [1]. It is defined as plasma sodium level below 135 mEq/litre. Many studies show that hyponatremia is prevalent in the hospitalized patients in around 20 percent. Incidence of hyponatremia is higher among elderly, when compared to young adults. This is attributed to the fact that, when elderly persons are exposed to a change in environment and an altered dietary
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MASTER CHART

ID	Age	Sex	HT	DM	CAD	TB	Hypothyroidism	CKD	Diuretics	NSAIDs	Fluoxetine	Headache	Nausea	Vomitting	Diarrhea	muscle weakness	muscle cramps	Malaise	Altered sensorium	Seizures	Coma
1	65	M	N	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	Y	Y	N	N
2	78	M	Y	Y	Y	N	N	N	N	N	N	N	Y	Y	N	N	y	Y	N	N	N
3	66	M	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N
4	81	M	N	N	N	N	N	N	N	N	N	N	Y	Y	N	N	N	Y	Y	N	N
5	75	M	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N
6	66	F	N	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	Y	N	N	N
7	79	F	N	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N
8	68	M	Y	Y	N	N	N	Y	N	N	N	N	Y	N	N	N	N	Y	Y	N	N
9	84	F	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N
10	69	F	Y	N	N	N	N	N	N	N	N	N	Y	Y	Y	N	Y	Y	Y	N	N
11	72	M	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N
12	72	F	Y	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N	Y	N	N	N
13	67	M	Y	N	Y	N	N	N	N	N	N	Y	Y	Y	N	N	N	Y	N	N	N
14	72	F	N	Y	N	N	N	N	N	N	N	N	N	N	Y	N	Y	Y	N	N	N
15	66	M	Y	N	Y	N	N	N	Y	N	N	N	N	N	N	N	N	Y	N	N	N
16	70	M	Y	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	Y	N	N	N
17	73	M	Y	N	Y	N	N	N	N	N	N	N	Y	N	N	N	N	Y	N	N	N
18	65	F	Y	Y	N	N	Y	N	N	N	N	N	N	N	N	N	Y	Y	N	N	N

19	72	F	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N	N
20	66	M	Y	N	N	N	N	N	N	N	N	N	N	Y	Y	N	N	N	Y	N	N	N
21	65	M	N	N	N	N	N	N	N	N	N	N	Y	Y	N	N	N	N	Y	N	N	N
22	72	M	Y	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	Y	Y	Y	N
23	82	M	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N
24	72	M	N	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	Y	N	N	N
25	66	F	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N
26	68	M	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N
27	77	F	Y	Y	N	N	N	N	Y	N	N	N	Y	N	N	N	N	N	Y	N	N	N
28	68	M	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N
29	76	F	Y	N	N	N	N	N	N	N	N	Y	Y	N	N	N	N	N	N	Y	N	N
30	66	M	Y	Y	N	N	N	N	N	N	N	N	Y	Y	N	N	N	N	Y	Y	N	N
31	79	F	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N
32	65	M	Y	N	N	N	N	N	N	N	N	N	Y	y	N	N	N	N	Y	Y	N	N
33	66	M	N	Y	N	N	N	N	N	N	N	N	Y	Y	N	N	N	N	Y	Y	N	Y
34	72	F	N	Y	N	N	N	N	N	N	N	N	Y	Y	N	N	N	N	N	N	N	N
35	66	F	N	N	N	N	N	N	N	N	N	N	Y	Y	N	N	Y	Y	Y	N	N	N
36	75	M	Y	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	Y	N	N	N
37	69	F	Y	N	Y	N	N	N	N	N	N	N	Y	N	N	N	N	N	Y	N	N	N
38	65	M	Y	N	N	Y	N	N	N	N	N	Y	N	N	N	N	N	N	Y	Y	N	N
39	86	M	N	N	N	N	N	N	Y	N	N	N	Y	Y	N	N	Y	Y	Y	N	N	N
40	77	F	Y	N	N	N	N	Y	N	N	N	N	Y	N	N	N	N	N	Y	N	N	N
41	78	F	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	N	Y	Y	Y	N	N	N
42	65	M	N	N	Y	N	N	N	N	N	N	Y	N	N	N	N	N	N	Y	Y	N	N
43	68	F	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N	Y	Y	N	N
44	75	M	Y	N	N	N	N	Y	N	N	N	N	Y	Y	N	N	N	N	Y	Y	N	N
45	66	F	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	Y	Y	Y	Y

46	72	M	Y	N	N	N	N	N	N	N	N	N	Y	Y	N	N	N	Y	Y	N	N
47	67	F	N	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	Y	Y	N	N
48	65	M	Y	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	Y	N	N	N
49	67	M	N	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y
50	78	F	Y	N	N	N	N	N	N	N	N	Y	Y	Y	N	N	N	Y	Y	N	N
51	82	F	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N
52	74	F	Y	N	N	N	N	N	Y	N	N	N	N	N	N	N	N	Y	Y	N	N
53	82	M	N	Y	Y	N	N	N	N	N	N	N	Y	Y	N	N	N	Y	Y	N	N
54	91	M	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	Y	Y	N	Y
55	69	F	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	N
56	68	M	Y	N	Y	N	N	N	Y	N	N	Y	N	N	N	N	N	Y	N	N	N
57	74	F	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N
58	78	M	Y	N	N	N	N	Y	N	N	N	N	N	N	N	N	N	Y	Y	N	N
59	73	M	N	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	Y	N	N	N
60	84	M	N	N	N	N	N	N	N	N	N	Y	Y	Y	N	N	N	Y	Y	N	N
61	74	F	Y	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N	Y	Y	Y	N
62	70	M	Y	N	N	N	N	N	N	N	N	Y	Y	N	N	N	N	Y	Y	N	N
63	65	M	N	N	N	N	N	N	N	N	N	Y	Y	N	N	N	N	Y	N	Y	N
64	68	F	N	N	Y	N	N	N	N	N	N	Y	N	N	N	N	N	Y	Y	N	N
65	78	F	N	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	Y	N	N	N
66	69	M	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	N	N
67	74	M	Y	N	Y	N	N	N	Y	N	N	N	Y	N	N	N	N	Y	Y	N	N
68	67	F	Y	N	N	Y	N	N	N	N	N	N	Y	N	N	N	N	Y	N	N	N
69	65	F	Y	Y	N	N	N	N	N	N	N	Y	N	N	N	N	N	Y	N	N	N
70	70	F	Y	Y	N	N	N	Y	Y	N	N	N	N	N	N	N	N	Y	N	N	N
71	71	M	N	N	Y	N	N	N	N	N	N	Y	Y	Y	N	N	N	Y	N	N	N
72	76	F	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N

73	65	F	N	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	Y	N	N	N
74	84	M	Y	N	Y	N	N	N	N	N	N	Y	Y	Y	N	N	N	Y	Y	N	N
75	74	M	N	Y	N	N	N	N	N	N	N	Y	Y	N	N	N	N	Y	Y	N	N
76	81	M	Y	Y	N	N	N	N	N	N	N	N	Y	Y	Y	N	N	Y	Y	Y	Y
77	67	M	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	N	N
78	74	M	N	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	Y	N	N	N
79	66	M	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	N
80	68	F	Y	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	N	N
81	66	F	N	Y	N	N	N	Y	Y	N	N	N	Y	Y	N	N	N	Y	Y	N	N
82	71	F	Y	N	N	N	N	N	N	N	N	Y	Y	N	N	N	N	Y	Y	Y	N
83	84	F	Y	N	Y	N	N	N	N	N	N	N	Y	N	N	N	N	Y	Y	N	N
84	74	M	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	Y	Y	N	N
85	86	M	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	N	N
86	72	F	N	Y	N	N	N	Y	N	N	N	N	N	N	N	N	Y	N	N	N	N
87	67	F	N	N	N	N	Y	N	N	N	N	Y	Y	N	N	N	N	N	N	N	N
88	66	M	N	Y	N	N	N	N	N	N	N	Y	Y	N	N	N	N	Y	Y	N	N
89	69	F	Y	N	N	N	N	N	N	N	N	N	Y	Y	Y	N	N	Y	N	N	N
90	67	M	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	N	N
91	83	M	N	Y	N	N	N	N	N	N	N	N	Y	Y	N	N	N	Y	N	N	N
92	67	M	N	N	N	Y	N	N	N	N	N	N	Y	N	N	N	Y	N	N	N	N
93	67	F	N	N	N	N	N	N	N	N	N	N	Y	Y	N	N	N	Y	Y	N	N
94	76	M	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	N	N
95	90	F	N	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	Y	Y	Y	Y
96	76	M	N	N	Y	N	N	N	N	N	N	Y	Y	Y	N	N	N	Y	Y	N	N
97	72	F	Y	N	N	N	N	N	N	N	N	N	Y	Y	N	N	N	Y	N	N	N
98	65	M	N	Y	N	N	N	Y	N	N	N	N	N	N	N	N	N	Y	N	N	N
99	87	M	Y	N	N	N	N	N	N	N	N	N	N	N	Y	N	N	Y	Y	N	N

100	68	M	Y	N	N	N	N	N	N	N	N	Y	Y	N	N	N	N	Y	Y	N	N

ID	Age	Sex	S Na	Urea	BUN	Glucose	serum osmolality	Volume status	urine Na	Etiology	Duration	TFT	Cosyntrropin test
1	65	M	123	32	14.95	96	256.67	Hypervolemia	8	cirrhosis	2		
2	78	M	122	38	17.76	120	257.01	Hypovolemia	18	Gi loss	3		
3	66	M	129	26	12.15	98	267.78	Euvolemia	102	SIADH	6	N	N
4	81	M	124	31	14.49	125	260.12	Euvolemia	104	SIADH	4	N	N
5	75	M	131	20	9.35	76	269.56	Euvolemia	100	SIADH	30	N	N
6	66	F	131	16	7.48	70	268.56	Euvolemia	56	HYPOTHYROIDISM	15	Y	N
7	79	F	130	30	14.02	80	269.45	Hypervolemia	18	Cardiac failure	7		
8	68	M	120	44	20.56	76	251.57	Hypervolemia	46	Renal	4		
9	84	F	132	18	8.41	69	270.84	Euvolemia	100	SIADH	7	N	N
10	69	F	118	26	12.15	84	245.01	Hypovolemia	16	Gi loss	2		
11	72	M	119	32	14.95	120	250.01	Euvolemia	78	SIADH	6	N	N
12	72	F	129	30	14.02	110	269.12	Hypervolemia	34	Renal	4		
13	67	M	130	28	13.08	90	269.67	Euvolemia	78	SIADH	4	N	N
14	72	F	123	33	15.42	124	258.4	Hypovolemia	17	Gi loss	2	N	N

15	66	M	133	15	7.01	70	272.39	Hypovolemia	22	Diuretics	8		
16	70	M	128	45	21.03	120	270.18	Hypervolemia	43	Renal	5		
17	73	M	129	33	15.42	110	269.62	Hypervolemia	10	Cardiac failure	7		
18	65	F	131	33	15.42	113	273.78	Euvolemia	24	HYPOTHYROIDISM	30	Y	N
19	72	F	130	30	14.02	110	271.12	Euvolemia	77	SIADH	4	N	N
20	66	M	128	36	16.82	122	268.78	Hypovolemia	16	Pancreatitis	3		
21	65	M	126	42	19.63	122	265.79	Hypervolemia	18	Nephrotic	5		
22	72	M	128	40	18.69	126	269.68	Euvolemia	56	SIADH	2	N	N
23	82	M	130	32	14.95	120	272.01	Euvolemia	67	SIADH	15	N	N
24	72	M	134	15	7.01	72	274.5	Euvolemia	100	SIADH	12	N	N
25	66	F	132	20	9.35	88	272.23	Hypervolemia	14	Cardiac failure	8		
26	68	M	133	22	10.28	68	273.45	Euvolemia	89	SIADH	10	N	N
27	77	F	131	25	11.68	82	270.73	Hypovolemia	32	Diuretics	15		
28	68	M	131	28	13.08	124	273.56	Euvolemia	74	SIADH	12	N	N
29	76	F	122	32	14.95	120	256.01	Hypervolemia	36	Renal	5		
30	66	M	126	38	17.76	133	265.73	Euvolemia	66	Adrenal insuff	7	N	Y
31	79	F	134	16	7.48	76	274.89	Euvolemia	76	SIADH	14	N	N
32	65	M	119	24	11.21	111	248.17	Hypovolemia	32	RTA	3		
33	66	M	118	34	15.89	115	248.06	Hypervolemia	16	cirrhosis	2		
34	72	F	127	40	18.69	180	270.68	Hypervolemia	22	Renal	4		
35	66	F	124	38	17.76	112	260.57	Hypovolemia	18	Gi loss	2		
36	75	M	128	35	16.36	116	268.29	Hypervolemia	28	Renal	5		
37	69	F	132	32	14.95	80	273.78	Hypervolemia	15	Cardiac failure	6		
38	65	M	132	33	15.42	78	273.84	Euvolemia	98	SIADH	15	N	N
39	86	M	116	39	18.22	88	243.4	Hypovolemia	38	Diuretics	2		
40	77	F	126	47	21.96	87	264.68	Hypervolemia	56	Renal	3		
41	78	F	124	40	18.69	114	261.01	Hypovolemia	13	Gi loss	2		

42	65	M	122	35	16.36	98	255.29	Euvolemia	76	SIADH	3	N	N
43	68	F	126	38	17.76	92	263.45	Hypovolemia	8	Gi loss	3		
44	75	M	130	45	21.03	112	273.73	Hypervolemia	45	Renal	5		
45	66	F	108	39	18.22	115	228.9	Euvolemia	76	SIADH	1	N	N
46	72	M	121	35	16.36	123	254.68	Hypovolemia	14	Gi loss	4		
47	67	F	118	46	21.5	112	249.9	Hypervolemia	56	Renal	4		
48	65	M	134	18	8.41	68	274.78	Euvolemia	66	SIADH	9	N	N
49	67	M	108	84	39.25	190	240.57	Hypervolemia	35	Renal	1		
50	78	F	118	37	17.29	114	248.51	Hypovolemia	12	Gi loss	3		
51	82	F	134	14	6.54	78	274.67	Euvolemia	87	SIADH	7	N	N
52	74	F	130	36	16.82	80	270.45	Hypovolemia	45	Diuretics	15		
53	82	M	122	42	19.63	45	253.51	Hypervolemia	45	Renal	4		
54	91	M	108	35	16.36	100	227.4	Euvolemia	78	SIADH	1	N	N
55	69	F	114	57	26.64	178	247.4	Hypervolemia	56	Renal	4		
56	68	M	129	27	12.62	121	269.23	Hypovolemia	65	Diuretics	12		
57	74	F	133	20	9.35	75	273.51	Euvolemia	67	SIADH	9	N	N
58	78	M	124	56	26.17	121	264.07	Hypervolemia	43	Renal	3		
59	73	M	129	34	15.89	111	269.84	Euvolemia	54	SIADH	6	N	N
60	84	M	132	21	9.81	78	271.84	Hypovolemia	12	Gi loss	2		
61	74	F	109	78	36.45	167	240.3	Hypervolemia	53	Renal	2		
62	70	M	116	35	16.36	120	244.51	Euvolemia	88	SIADH	3	N	N
63	65	M	126	34	15.89	121	264.4	Euvolemia	45	CARBEMAZEPINE	8	N	N
64	68	F	119	28	13.08	86	247.45	Euvolemia	97	SIADH	2	N	N
65	78	F	132	33	15.42	78	273.84	Euvolemia	45	FLUOXETINE	20	N	N
66	69	M	121	65	30.37	156	261.51	Hypervolemia	53	Renal	1		
67	74	M	126	23	10.75	122	262.62	Hypovolemia	28	Diuretics	5		
68	67	F	134	12	5.61	80	274.45	Euvolemia	66	SIADH	14	N	N

69	65	F	132	14	6.54	120	273	Euvolemia	76	SIADH	8	N	N
70	70	F	130	45	21.03	129	274.68	Hypovolemia	45	Diuretics	4		
71	71	M	129	28	13.08	114	269	Hypovolemia	8	Gi loss	12		
72	76	F	133	20	9.35	74	273.45	Euvolemia	76	SIADH	8	N	N
73	65	F	132	21	9.81	100	273.06	Euvolemia	26	HYPOTHYROIDISM	37	Y	N
74	84	M	120	24	11.21	126	251	Hypervolemia	14	Cardiac failure	4		
75	74	M	122	28	13.08	140	256.45	Euvolemia	88	SIADH	4	N	N
76	81	M	105	29	13.55	180	224.84	Hypovolemia	15	Gi loss	2		
77	67	M	123	34	15.89	125	258.62	Hypervolemia	17	Cardiac failure	5		
78	74	M	134	16	7.48	70	274.56	Euvolemia	67	SIADH	20	N	N
79	66	M	132	18	8.41	80	271.45	Euvolemia	56	SIADH	12	N	N
80	68	F	129	20	9.35	126	268.34	Hypervolemia	18	Cardiac failure	3		
81	66	F	129	48	22.43	138	273.68	Hypovolemia	45	Diuretics	7		
82	71	F	118	35	16.36	110	247.95	Euvolemia	64	SIADH	2	N	N
83	84	F	121	25	11.68	112	252.39	Hypovolemia	12	Gi loss	3		
84	74	M	116	54	25.23	100	246.57	Hypervolemia	55	Renal	2		
85	86	M	120	34	15.89	88	250.56	Euvolemia	76	SIADH	4	N	N
86	72	F	129	53	24.77	125	273.79	Hypervolemia	55	Renal	8		
87	67	F	131	21	9.81	80	269.95	Euvolemia	45	HYPOTHYROIDISM	32	Y	N
88	66	M	127	37	17.29	100	265.73	Euvolemia	75	SIADH	3	N	N
89	69	F	124	38	17.76	112	260.57	Hypovolemia	6	Gi loss	4		
90	67	M	126	54	25.23	115	267.4	Hypervolemia	56	Renal	4		
91	83	M	124	34	15.89	123	260.51	Hypovolemia	8	Gi loss	4		
92	67	M	129	36	16.82	115	270.4	Euvolemia	93	SIADH	7	N	N
93	67	F	126	32	14.95	121	264.06	Hypovolemia	12	Gi loss	3		
94	76	M	129	45	21.03	145	273.57	Hypervolemia	45	Renal	5		
95	90	F	110	48	22.43	124	234.9	Hypervolemia	34	Renal	4		

96	76	M	122	23	10.75	112	254.06	Hypovolemia	14	Gi loss	4		
97	72	F	132	24	11.21	88	272.89	Euvolemia	86	SIADH	5	N	N
98	65	M	129	50	23.36	143	274.29	Hypervolemia	43	Renal	7		
99	87	M	123	23	10.75	122	256.62	Hypovolemia	14	Gi loss	4		
100	68	M	133	14	6.54	102	274	Euvolemia	76	SIADH	6	N	N